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THE CAUSES OF DISEASE

By MOGENS FOG

Current medical science — which we are pleased to call rational — is so dominated by research into the causes of disease, that it may well seem superfluous, perhaps impossible, to treat the problem in a general way.

The past ten years have, nevertheless, witnessed increasing interest in medical circles in the fundamentals of causality.

There are several reasons for this.

Firstly: The more we get to known about a disease due to improvements in our methods of examination, the more factors we have to work with. Every new link in the causal chain proves to be conditioned by a multiplicity of factors which do not just act "linearly", but are mutually dependent. This is true both of the pathological processes in the individual organism, and of the external factors. Furthermore, external and internal factors likewise interact.

Probably no disease is any longer regarded as the result of a single agent. Pathological manifestations arise due to a plurality of integrated conditions.

This alone makes it desirable to systematise and clarify the basic principles.

Secondly: The modern natural sciences, in which I include medicine, are so dominated by the amassing of facts, that one often loses track of the synthesis — in fact, syntheses are sometimes even treated with suspicion.

F. M. R. Walshe, among others, has commented on the situation in the preface to his excellent book "Critical Studies in Neurology": ".... the unresting collection of new facts in science is to so relatively slight a degree accompanied, or illumined, by critical assessment and synthesis of all this new information, or at least by some deliberate search after synthesis. Here, surely, integration is not keeping pace with differentiation".

He continues: ".... For too many amongst us, also, the inadequate conception that "science is measurement" and concerns itself with nothing but the metrical has become a thought-cramping obsession".

Similar considerations have recently led research workers to attempt to sketch the framework of the medical universe, or at least bits of it — to try to find some basic principles which may help them order the mass of medical phenomena.

Thirdly, and lastly: The epistemological discussions arising out of the recent developments in physics, have undoubtedly stimulated the desire for similar general causal principles in other sciences, including medicine. Decisive discoveries in one science always make their mark on general epistemology.

It is necessary to stress, however, that it is not permissible to draw parallels between the "indeterminism" of the basic physical phenomena and the phenomena biology investigates — at least not at the present stage of biology. Attempts to transpose the philosophical consequences of modern physics to such problems as the relationship between mind and body must be regarded as pure speculation.

The only debt medicine owes to physics in this respect is the stimulant which has made us delve more deeply into our own, completely different, problems of cansality.

One may well ask whether there is any need to classify the known causes of disease systematically. Is it not sufficient just to study the causes of the individual disease, taking not only the purely medical, but also other factors into account?

Personally, I consider it would be very practical if we could find some general principles for etiological classification. We could then more easily survey and compare the causes of several, perhaps of all diseases in spite of their differences in other respects. In this manner it would be easier for the various branches of our dangerously specialised science to understand and help each other. One should not underestimate the value which even mere terminological aid may have

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Lecture at the Medical School, Cambridge, October 1957. From the Dept. of Neurology, Rigshospitalet, University of Copenhagen. Head: Prof. *M. Fog.*

in this respect. Apart from this, however, such a survey also may help ensure that less conspicuous etiological factors are not neglected.

Whether or not such a classification is of value will depend not on its logical impeccability, but on its ability to help us achieve these two goals: Principal comparison of the causes of different diseases; and systematic search for all possible causes in a particular disease. This pragmatic criterion I shall use to evaluate some of the etiological "systems", previously presented.

SOME PREVIOUS ETIOLOGICAL SYSTEMS

The most well-known one was presented at the conference held by The Public Health Association of New York City in 1950, and published under the title "Tomorrow's Horizon in Public Health".

The general principles are described by John E. Gordon in his contribution entitled "The newer epidemiology". Gordon refers to a remark made by Winslow in an editorial in The American Journal of Public Health to the effect that ".... the tubercle bacillus [is] not the cause of tuberculosis, but .... one of the causes".

Gordon's etiological system is purely epidemiological, though taken in the widest sense of "communicable disease" to refer to medical ecology — diseases affecting human groups and societies.

Three main classes of factors interact: 1) the host, 2) the agent of disease and 3) the intricate environmental complex. This finding requires that all factors entering into disease production and disease distributions be kept in view at the same time, and each in relation to the other.

The factors are grouped in a general scheme:

Agent of disease
- Physical
- Chemical
- Biological

Host factor
- Inherent
- Acquired

Environment
- Physical
- Biological
- Social

In his contribution to the conference: "Nutrition in the light of the new epidemiology" H. D. Kruse made use of Gordon's principles but elaborated into more than 60 head- and subdivisions, a list which is declared "not exhaustive". This is in my opinion an exaggeration in details which deprives a classification of any practical usefulness.

Gordon's classification undoubtedly possesses several advantages, chief among which is its basic simplicity and its undeniable usefulness when applied to communicable diseases, including dietary diseases. But his system is restricted to the so-called exogenous diseases, and it fails to take into consideration the mutual interaction of factors active in the bodily or internal environment, the importance of the duration of their effects, or their respective relationship to the external environment.

The practical value of Gordon's system is consequently limited.

As an example of systematic causal descriptions including the internal milieu factors we may take Karl Birnbaum's psychiatric structural analysis (Die Strukturanalyse als klinische Forschungsprinzip, 1920. Der Aufbau der Psychose. Berlin, 1923).

According to Birnbaum, psychiatric diseases are clinically often dominated by unspecific, unessential elements, whose pathoplastic effects depend on the individual's preformed traits of personality and the like. These pathoplastic effects may conceal the more important fundamental pathogenetic elements.

Birnbaum believes that it is necessary always to trace four sets of factors no matter what disease one studies, namely: the pathogenetic ("ursachlische"), the predisposing (preparatory), the preformative ("vorbildend") and the provocative (releasing).

All these factors must be taken into consideration in all their various forms. With truly Germanic linguistic talent, Birnbaum burdens them with the qualities: polymorph, heteromorph, polygenetic, heterogenetic, polyvalent and heterovalent.

Quite apart from what one might think of Birnbaum's terminology, his "system" very aptly pinpoints some important factors determining the manifestations and frequency of disease. The pathogenetic and the provocative factors decide whether or not a disease will occur in a particular individual, while the predisposing and preformative factors decide its particular course and clinical picture — give it its pathoplastic features.

Birnbaum's classification thus provides us with a description of the interaction of the causes of disease, their integration; but two important factors are completely neglected: The essential cause of the disease — the factor that determines the type of disease — which Gordon calls the agent of disease, and the interaction between the host and the external environment.

A third example of such causal schemes, also taken from psychiatry, is Strömgren's (1940), which classifies diseases as traumonome, eidonome and idionome.

Traumonome refers to cases where a particular noxious agent, either endogenous or exogenous, is the sole factor deciding both the occurrence and the clinical manifestations of a psychosis. Examples of this are rabies, cocaine and mescaline intoxications.

Eidonome reactions comprise the psychotic reactions which, although they are similar in nature

no matter the individual affected, have different causes. Donhoeffer's exogene reaction types and the severe dementias may serve as illustrations.

Idionome reactions are determined by the individual, internal environment alone. This milieu is partly a product of heredity, partly of the effects of the life the individual has led. The psychosis seems to appear without any specific noxious agent, and provocatives play only a minor role, as they do not lead to psychoses in other individuals. As examples one may mention catathymic, psychogenic psychoses whose content and mode of manifestation are determined purely by individual factors.

This classification is of undoubted value, not only for rough discrimination between the various psychoses, but also, and in particular, because it provides us with an impetus to differentiate between the traumonome, eidonome and idionome factors in the individual case's pathogenesis. Strömgren's classification may furthermore be of value when dealing with the somatic diseases. It can, however, not be applied to diseases in general, as its purpose is far too specialised.

PROPOSED ETIOLOGICAL CLASSIFICATION

When attempting to describe etiological classification principles it is necessary to ensure that they fulfill the demand for expediency which I mentioned previously — the system must be able to help us compare all sorts of different diseases at the same time as it pinpoints concrete etiological problems. It is necessary to consider the relationship between the agent of disease, external and internal environment, exogenous and endogenous factors, psychogenesis and somatogenesis, and genetic, permanent as well as temporary factors. One must consider their constancy and variability, their basic characteristics and their specific appearance, as well as their interrelationships.

One cannot possibly satisfy these demands without running the risk of either simplifying matters so much that the result is without practical value because it is so general, or on the other hand, that the "system" becomes so complicated in its attempt to include detail that it is confusing, cf. Kruse's scheme.

The attempt at classifying the causes of disease, which I shall now describe, has probably not managed to avoid the dangers of both extremes. I hope, however, that it does pay more attention to the multiplicity and interaction of the various etiological factors than previous classifications have done.*)

*) The classification principles were presented and elaborated in discussion groups in connection with the Northern Summer University, Askov, Denmark, 1950, where the subject was: Problems of Causality. I am indebted to numerous participating colleagues for their contributions to the evaluation in general and in special fields.

ETIOLOGICAL FACTOR GROUPS

1. *Constitution* — or better: *reaction preparedness.*
   By this I understand permanent individual factors, partly genetic, partly acquired. On the one hand we have the hereditary traits or genotypic factors, and on the other, the phenotypical characteristics arising from the interaction between the environmental stimuli and the hereditary or congenital constitution of the organism.

2. *Environmental factors.* (Milieu factors.)
   These factors may belong to the internal or the external environment. In principle, they exert an effect only so long as they are actually present in or outside the organism. Yet they are so related to the constitutional factors that they are able to affect the "host" permanently if they are sufficiently strong or act over a long enough period, especially during the organism's formative years. They may prepare the ground for the

3. *Precipitating factors.*
   By "precipitating factors" I understand temporary deviations from normal environmental conditions, either internal or external, which decide when the disease will manifest itself — one might call them unspecific, chance causes. They may, nevertheless, be so strong or of such a type that their after-effects remain as internal environmental, or even constitutional, factors.

4. *Specific factors.*
   The specific factor decides the nature of the disease and its nosological characteristics. The specific factor is, in other words, *necessary* if the disease concerned is to occur, but it is not always *sufficient* to cause the disease — in fact it is probably rarely able to cause the disease on its own.

Let me specify these four groups in greater detail by means of some banal examples, and then try to test the value of the "system" by applying it to various diseases. It will be demonstrated that not all factors are active or equally active in all disease.

1. The definition of *constitution* or *reaction preparedness* is very similar to several other previous definitions, although I have been unable to find a completely satisfactory one.

It is, presumably, unnecessary to go into greater detail with regard to the hereditary disposition.

When certain diseases occur in connection with a particular body build more frequently than together with others as, for example, in the case of leptosomia and schizophrenia, this by no means implies that this genetic, somatic factor is a necessary cause of the disease. The factor body build is hereditary, but may well be merely predisposing. Something similar is true of the relationship

between the mental "hereditary milieu" and manifest neurosis.

As examples of acquired constitutional factors one may mention (a) how apt the kyphoscoliotic is to acquire pulmonary tuberculosis, (b) induced or acquired immunity to infectious diseases, (c) the role played by childhood environment as regards later reactions to mental trauma, and so on.

If a disease manifests itself familially with a frequency corresponding to the Mendelian distribution independently of environmental factors, its occurrence is purely genetically determined — as for example Huntington's chorea. The genetic factor is consequently identical with the specific factor. The disease is idionome, in Strömgren's terms.

If an infectious disease rarely or never occurs twice in the same person, for example varicella, then the immunity constitutes part of the persons "reaction preparedness" — it is, once aquired, a permanent element of his constitution.

If a disease occur in all, or nearly all the persons exposed to its specific agent, such as German measles in a virgin area as Greenland, then constitutional factors, as well as environmental and precipitating factors, are of no importance, and the picture is completely dominated by the specific factor. It is traumonome, according to Strömgren.

2. *Environmental factors.* By "environmental" or "milieu" factors I mean both external and internal causal elements. As for the external environment, I choose some experiences from the morbidity in the German concentration camps during the last war.

There was an extraordinary high incidence of tuberculosis among former inmates in the camps after their repatriation. The weakened resistance due to poor nutrition, etc., meant that people were infected who under normal conditions would have resisted infection effectively. The temporary environment predisposed unspecifically to the specific infection.

Some former prisoners seem not to have been infected during their stay in Germany but the after-effects, their continued general weakness after returning home, favoured a later infection by the tubercle bacillus, once they were exposed to it. To speak in terms of the scheme: outer environmental factors in this case were more or less permanently transposed into predisposing inner milieu factors.

Another environmental factor was the close contact between the prisoners, packed as they were into grossly inadequate barracks, whereby they were exposed to a considerable greater risk of infection than under normal conditions. This external environmental factor was, of course, only active as long as the persons lived in the particular surroundings.

Further one may mention the so-called famine-disease and its consequences. The famine-disease, according to available data, is due to the very low protein-content of the camp diet. This lack of protein must be regarded as the specific factor. Naturally it is part of the extraordinary environment the prisoners were exposed to; all exogenous disease agents are part of the environment. But it was a particular and not an unspecific, predisposing external factor.

The tubercle bacillus was a specific agent which became pathogenetic because of the general bad conditions. The lack of protein was a specific agent contained in the particular external milieu, — an environment which besides unspecifically favoured the occurrence of various other diseases.

The internal environment or milieu arising due to a disease or an abnormal condition, may often predispose a patient or reduce his resistance to completely different pathogenic agents.

In this connection I can mention the relationship between achylia and pernicious anemia. By no means all patients with achylia develop pernicious anemia. But the lack of gastric hydrochloric acid leads to alterations in the flora of the upper part of the small intestine, which in connection with a lack of the intrisic factor, the specific agent in pernicious anemia, prevent the resorption of B_{12}.

Without achylia no anemia develops, but achylia is only an inner milieu factor which conditions the action of the directly pathogenic factors.

One may object that once acquired, achylia is irreversible, and so is not an internal milieu factor in our definition but has entered into the permanent reaction-preparedness. Perhaps it is better to exemplify the matter by the increased tendency to fracture in patients with rickets. The specific agent, the trauma, if it is of a certain intensity, will cause a fracture only as long as there is a low calcium content of the bones. Once the rickets are cured, a similar trauma will not cause fractures.

3. *Precipitating factors.* When someone has long been exposed to tubercle infection and contracts tuberculosis during an attack of influenza, the influenza must be regarded as the precipitating agent. When someone in a state of acute depression consequent to a mental trauma fails to take usual care in the street and is knocked down, his momentary mental state is responsible for precipitating the accident. (In this respect I do not refer to the accident-prone persons where constitutional factors appear to predispose to their frequent accidents in circumstances where others rarely are injured).

It is important, I believe, to separate precipitating factors from the general environmental factors just mentioned, as they are characteristically short-lived and highly "unspecific".

4. *Specific factors.* I have not chosen my many examples from the infectious diseases by chance. The bacteriological developments of the latter

part of the 19th century were instrumental in initiating the belief that every disease had its own special cause. Research into the avitaminoses at the beginning of this century strengthened this dogma, and even today there are a number of diseases whose causes we know that are regarded as monistically determined — such as Huntington's chorea, to take a genetic example.

Medical thinking has only gradually been able to free itself from this point of view. Only gradually it has realised that although there may be a specific cause, one must also search out the conditions that make it possible for a disease to manifest itself.

As pointed out in the introduction, this approach gave rise to the desire to systematise.

Etiological classifications can naturally only codify known facts. Nevertheless I hope that the principles I have sketched show that it is advantageous to describe the active disease agents as a continuous process of integration.

The "system" seeks to make clear that specific agents of disease are only rarely both necessary and sufficient causes; diseases occur as the result of a number of interacting factors, each of which acts more or less intensely and more or less constantly. In the individual case, when and how the disease manifests itself depends — to put it very simply — on the sum of all these factors. Should all the non-specific conditions be present, a virus or trauma or the like of comparatively minor intensity may exert an effect, which it would not have were one or more of the adequate constitutional, environmental or precipitating factors absent. If the necessary hereditary conditions for a disease — for example goiter — are sufficiently prominent, it may manifest itself without other factors being present. On the other hand, weaker predispositions to goiter will only give rise to symptoms when the patient is subjected to special stress.

EXAMPLES OF APPLICATION

In order to test the etiological classification here described, I shall apply it to some diseases of widely different character. This test will illuminate whether the system is able to provide a useful framework for future etiological research.

Diabetes mellitus. The known etiological agents comprise: (1) heredity, (2) endocrinological factors, (3) adiposity, (4) various factors such as race, sex, infection, pancreatitis, etc.

The genetic factors manifest themselves in the form of increased specific morbidity among family members, concordant manifestation in uniovular twins and recessive heredity of the disease.

Genetic factors are presumably the specific agents necessary to produce the disease when exceptional "exogenous" conditions such as pancreatitis are disregarded.

But when one observes that this disease is more common among women than among men, the problem arises as to whether this is due to genetic or to environmental factors: whether or not the disease frequency varies according to the frequency of adiposity which is supposed to be higher in women. This question can be made the subject of research. I admit that I do not know whether such an investigation has been carried out. But if there is prevalence of diabetes in women in a material excluding adipose patients, then the genetic factor plays the predominant role, not the acquired factor, the adiposity.

There is no doubt whatsoever that adiposity is related to diabetes, yet even so it is necessary to define this relationship more precisely. Depend adiposity and diabetes simply on coexistent linked constitutional genetical factors or is adiposity a mere environmental element? The prophylactic problems are naturally different in each case. It seems possible to elucidate this matter by examining whether the frequency of diabetes in predisposed families can be reduced by preventing adiposity. It should be remembered that the incidence rate of diabetes can be prophesied very accurately on the basis of a family case history.

A similar study can be carried out with regard to the classification of endocrinological disorders occurring more frequently in diabetic patients than on the average.

Finally, I may point out that it should be possible to determine the role of infection and trauma as precipitating agents where one has exact knowledge of the probable morbidity. If a presumably *latent* host develops diabetes following brief exposure to such exogenous environmental factors, this implies that he is not a *purely* latent host, but may be affected by certain circumstances so that he develops the disease — which may be important from the point of view of insurance.

I am not a diabetes expert. My suggestions may well be erroneous. But they are only intended to exemplify the possible use of the described etiological "system", when planning research into the causes of diseases.

I should like to make similar reservations about the other examples I am about to present.

Puerperal psychoses. Within 6 months of having given birth to a child, more women manifest psychoses than women of similar age-groups who have not born a child. a) The psychoses appear more frequently in connection with complicated births than after births without complications. b) Most women who develop puerperal psychoses have feared or hated the prospect of giving birth to a child — only a few seem to have looked forward to the event. c) Finally, there are more puerperal psychotic patients with manic-depressive family members or previous manic-depressive episodes than is usual for women of the same age-groups and with the same stress.

One particular factor is necessary if such a psychosis is to appear, namely the experience of

birth. It is nevertheless impossible to regard this experience as a specific cause of the psychosis — the experience of birth is far too general for this.

Complications are more frequent than normal delivery — but puerperal psychoses do develop without there being complications, so complications are not a necessary factor although they may be contributive.

The attitude most of these patients adopt toward pregnancy and birth may, so to speak, be reasonable and understandable from the point of view of their previous and present conditions of life. In which case it is to be treated as an environmental factor. On the other hand, it may be due to their particular personality, and must consequently be classed as constitutional. I do not know whether anyone has tried to decide between these two possibilites, but surely it is worthwhile investigating the matter, not least because of its prophylactic implications.

The prevalence of manic-depressively disposed patients among those suffering from puerperal psychoses seems definitely to indicate a predisposing constitutional factor, although it is not alone sufficient or necessary for the appearance of the disease.

Thus it is possible to point out and to a certain extent classify a number of important etiological factors, though none of them is sufficient to cause the disease, even in combination with others. The analysis emphasises that we as yet know nothing about the finally decisive factors of this psychosis.

Poliomyelitis. The problems we encounter here are the same as for so many other diseases of infectious nature: We know what the causal agent is, but we do not know the reasons for the seasonal variations in manifestation, and neither do we know why only a few and not all exposed persons contract the disease during an epidemic. Without going into detail, I should like to mention a few points of immediate interest.

It is impossible to explain the distribution of poliomyelitis by the distribution of the virus: the virus is very common in countries such as the South American where poliomyelitis is comparatively rare. This fact, together with our present knowledge about the effectiveness of vaccination, indicates that acquired immunity — *i. e.*, an acquired constitutional factor — plays an important part in deciding both the individual and the demographic distribution of polio.

The seasonal variations may *either* be due to differences in the virulence of the specific agent, *or* to fluctuations in the susceptibility of the population, *or* to the way in which the virus is transported. The latter possibility does not seem to be of any importance, however, as we know that the virus is present throughout the year.

During the epidemic in Denmark in 1952 it was shown that the virus is probably transported solely or mainly by means of contact with infants. If this holds true, then contact with such children during epidemics constitutes a decidedly important milieu factor.

Apart from this, it seems that tonsillectomy, smallpox vaccination, and other things reduce resistance to the disease, and may therefore act as *precipitating agents.* In addition, we must take into consideration the possibility that muscular fatigue as well as intramuscular injections may have some influence on what muscle-groups are liable to be paralysed if infection occurs — in other words, they act as special provocations.

Thus it seems possible to classify the known etiological parameters of poliomyelitis in accordance with the scheme I have proposed without much difficulty, and furthermore to clarify possible approaches for research into as yet unknown epidemiological determinants.

SOME ASPECTS OF ETIOLOGICAL RESEARCH

Similar analyses may be carried out for other infectious diseases. It is interesting to see that the bacteriological discoveries which led to the monistic approach, delegating a particular cause to each disease, have since inspired the approach that stresses etiological multiplicity.

The other main contribution to this modern etiological viewpoint came from dynamic psychiatry. The need for some form of systematisation has quite a different basis in psychiatry, however. Only for very few psychoses is it possible to identify a specific endogenous or exogenous agent. One is forced to operate with a number of more or less equally important elements which must interact in order to produce psychosis.

The question arises whether many of the clinical entities, be they somatic or mental, may rightly be termed "specific" in the sense that there is some single endogenous or exogenous agent which is necessary — although often not sufficient — to cause the particular symptom complex.

As far as I can judge, ideas like this are beginning to exert themselves in research on the "rheumatic" diseases, on cancer, and in the discussions about S e l y e's adaptation syndrome.

Even though one may be able to demonstrate that a number of various factors influence the manifestations of these groups of diseases, none among them is regarded as the primary cause, essentially deciding the nature of the disease. The symptoms are the result of the interplay of factors constituting the predisposing "milieu" — the interplay of the factors I have chosen to call constitutional, environmental and precipitating, — each of which is in itself unspecific.

But precisely because of this aspect of a both multiple and non-specific etiological concept in many fields of medicine, I believe that it is

expedient for medical research to attempt to isolate and group fundamentally each of the various causal elements.

Only in this way will it be possible to evaluate the importance of their duration, their relative weight, their interaction in the etiological causality pattern.

A systematic classification of etiological factors is not a mere philosophical aspect of medicine. It will, I believe, be helpful to research.

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ETIOLOGICAL FACTORS IN CEREBRAL PALSY AND THEIR CORRELATION WITH VARIOUS CLINICAL ENTITIES

By S. BRANDT and V. WESTERGAARD-NIELSEN

The clinical investigator who collects — from patients with cerebral palsy — information about abnormalities during pregnancy, birth and early childhood, will do this in order to find some indication of cause and etiology which might throw light on the possibilities for preventive procedures.

From available publications of such studies, one may conclude that only a minor group (in our material 13 per cent) of cerebral palsies have been acquired after the neonatal period. The main group (at least $^2/_3$ of the explored cases) apparently result from lesions operating either in utero or at the period surrounding the birth (Fig. 1a). As most such figures are barely related to a diagnosis of "cerebral palsy" and not to the various manifestations of the motor handicap, we found it of interest to correlate clinical sub-groups of cerebral palsy with the most likely time of injury, *i. e.* prenatal, paranatal or postnatal (Fig. 2), as well as with various more specified factors. We found that prenatal factors, including prematurity, were responsible for a comparatively large group of our spastic diplegias and this correlation was even higher (54 per cent) for symmetric diplegias and paraplegias than for asymmetric diplegias (41 per cent), both figures outnumbering the proportion in unselected material (36 per cent). Low figures for postnatal factors, only 5—6 per cent, were found in the same clinical subgroups, whereas such factors were frequent among spastic hemiplegias. For some reason postnatal factors were found in 32 per cent of the left hemiplegias and 16 per cent of the right, in other words, twice as common in the left as in the right hemiplegias.

Although the chance to unveil factors of potential etiological significance is to some degree dependable on the care adopted in collecting data, we still have to admit that in many case histories no suggestion of etiology can be found.

There will also be a group of cases, where two or more factors may each be more or less responsible for the lesion. Such facts are not accounted for in most statistics. We felt it necessary to place 20—25 per cent of our cases in this "cryptogenic"

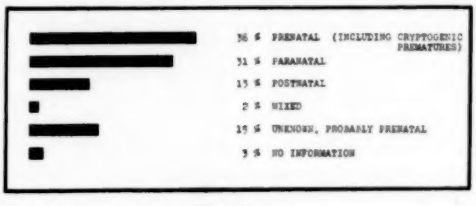

Fig. 1 a.

Most likely time of damage in relation to birth in 628 cases of cerebral palsy.

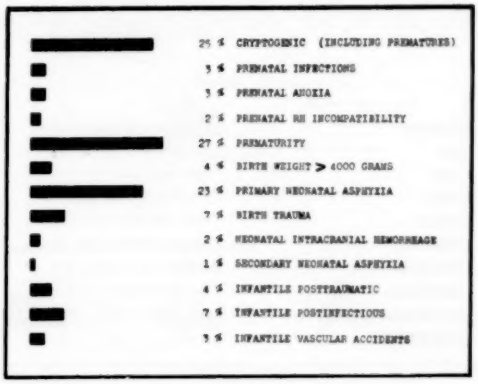

Fig. 1 b.

Frequency of various possible etiological factors (partly overlapping), elicited from case histories in 628 patients with cerebral palsy.

From the Cerebral Palsy Clinics at the Orthopedic Hospitals in Aarhus and Copenhagen, Denmark. Under the auspicies of the Society and Home for Cripples.

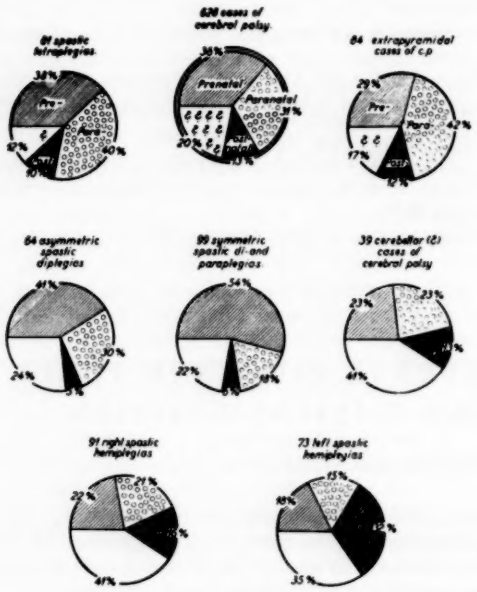

Fig. 2.
Distribution among pre-, para-, and postnatal injury in 628 cases of cerebral palsy and in various clinical subgroups.

group (Figs. 1 and 2). It may, however, be of further interest that factors giving us some idea of the time of injury were lacking, particularly in histories from spastic hemiplegias and from patients with cerebellar symptoms (Figs. 2 and 3). The screening between prenatal and paranatal factors will always be to some degree artificial. It can always be claimed that neonatal asphyxia may be the result of prenatal depression of respiratory centers and not necessarily a consequence of labor itself. Realizing this we have, nevertheless, for practical purposes grouped primary neonatal asphyxia as a paranatal factor. As shown in Fig. 2 paranatal injury seemed responsible for the main part of our spastic tetraplegias and our

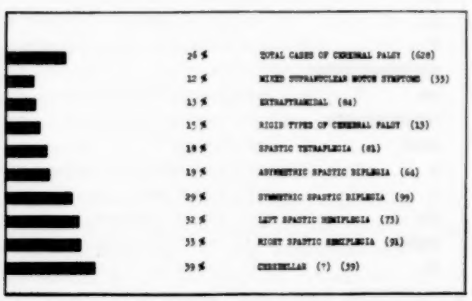

Fig. 3.
The ratio in which no information could be traced indicating etiology in 628 cases of cerebral palsy and in some clinical subgroups, each covering various numbers of patients as given in parenthesis.

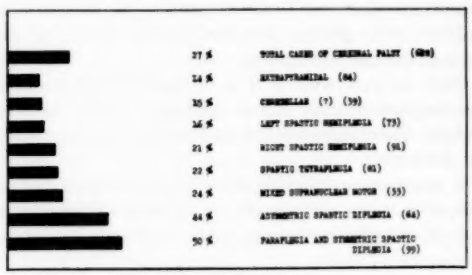

Fig. 4.
The ratio of neonatal prematurity in 628 cases of cerebral palsy and in some clinical subgroups, each covering various numbers of patients as given in parenthesis.

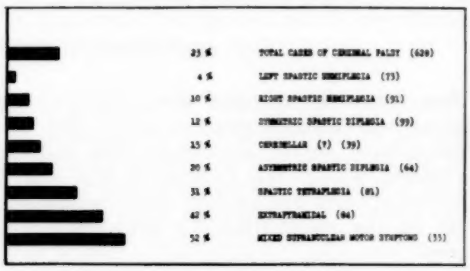

Fig. 5.
The ratio of information indicating perinatal anoxia in 628 cases of cerebral palsy and in some clinical subgroups, each covering various numbers of patients as given in parenthesis.

athetoids (extrapyramidal c. p.), namely 40 per cent and 42 per cent respectively.

Although several factors of potential etiological significance have been mentioned in our case histories from patients with cerebral palsies, most of them usually account for less than 7 per cent (see Table 1). Two factors, however, stand out with remarkably high values in c.p. children when compared with healthy children: *prematurity* with 27 per cent and *neonatal asphyxia* mentioned in 23 per cent of the histories. This is in agreement with earlier statistics, but our desire to correlate these factors with clinical subgroups gave us additional information of some interest. Thus, prematurity (Fig. 4) appeared to be three to four times as frequent (50 per cent) in symmetric spastic diplegias and paraplegias than in extrapyramidal hyperkinesias (14 per cent). In contrast, neonatal asphyxia was 3½ times commoner in this last group than among the symmetric spastic diplegias (Fig. 5). The overlapping of the two factors in these two groups of patients is less than would be expected from those who might have adopted the view that prematurity is a common predisposing cause of neonatal asphyxia (Fig. 6). On the other hand neonatal asphyxia is of negligible significance in spastic hemiplegias (right hemiplegia 10 per cent, left hemiplegia 4 per cent) (Fig. 5).

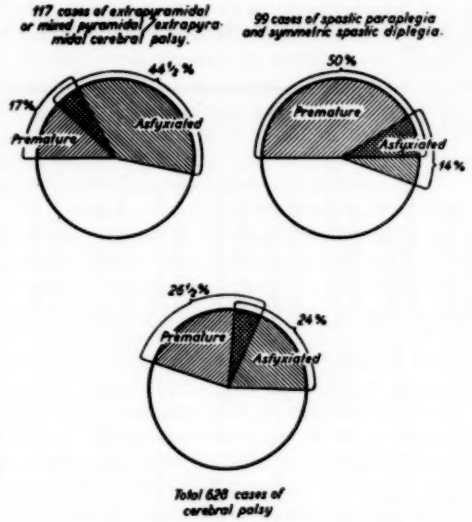

Fig. 6.

Frequency of prematurity and neonatal asphyxia in cerebral palsy and two clinical subgroups.

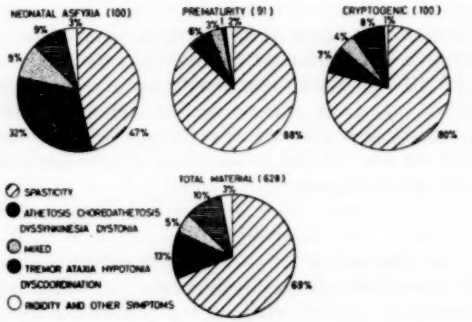

Fig. 7.

Dominating neurological symptom in 628 cases of C. P. as well as in three "pure" etiological subgroups.

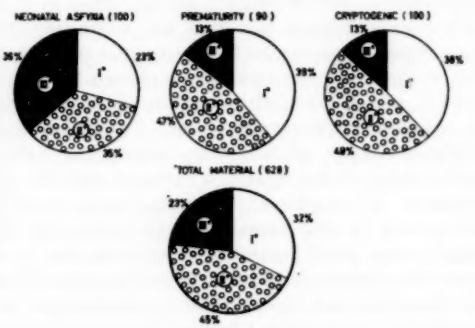

Fig. 8.

The degree of motor handicap in 628 cases of C. P. as well as in three "pure" etiological subgroups.

The exact neurological diagnosis of c.p. may be difficult during the first year of life. When neonatal asphyxia is the only etiological factor elicitable from the history there will be, however,

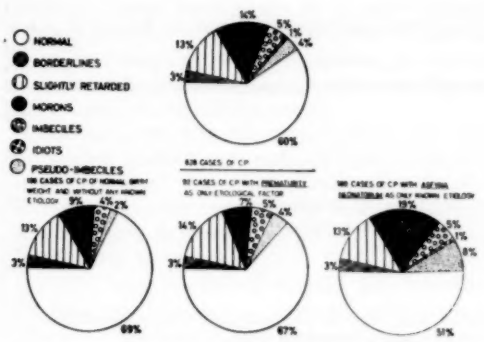

Fig. 9.

Frequency of mental retardation in 628 cases of C. P. as well as three "pure" etiological subgroups.

as seen from Fig. 7, a 32 per cent chance for an extrapyramidal and a 9 per cent for a mixed pyramidal/extrapyramidal type of c.p., whereas this risk — always involving a more crippling prognosis — is 6 and 3 per cent respectively where prematurity has been the only elicitable etiological factor. On the whole, a history of neonatal asphyxia involves a risk of a more serious motor handicap than does a history of prematurity as seen from Fig. 8. Finally, a smaller percentage of normal mental development was found in a group of c.p. children where neonatal asphyxia was the single known etiology, than in a similar group where prematurity was found as the only abnormality in the early history (Fig. 9). Prematurity was correlated with a smaller risk of epilepsy and electroencephalographic abnormalities, than neonatal asphyxia, and this last birth complication was closely correlated with speech disorders (Fig. 10).

Is is interesting that cases of spastic hemiplegia were on an average of a more obscure etiology, no factors being detectable in 32—33 per cent of the cases in contrast to 18—19 per cent for the spastic tetraplegias and the asymmetric spastic diplegias (Fig. 3). We have also been surprised to discover that a high birth weight, upon which

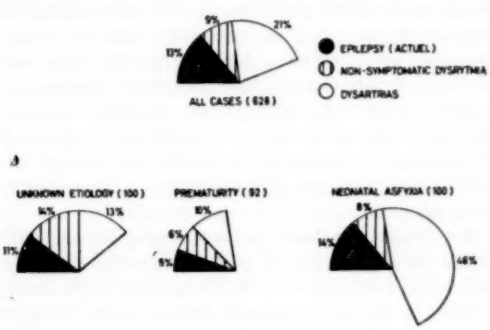

Fig. 10.

Frequency of present epilepsy, non-symptomatic dysrhythmias and dysarthrias in 628 cases of C. P. as well as in three "pure" etiological subgroups.

Table 1.
Frequency (percentage) of various factors of potential etiological significance in cerebral palsy and different clinical subgroups.
(Factors overlapping)

Figures of outstanding high or low values in italics.	All types of cerebral palsy (628)	Spastic tetraplegias (81)	Symmetric spastic diplegias (99)	Asymmetric spastic diplegias (64)	Right spastic hemiplegias (91)	Left spastic hemiplegias (73)	Extrapyramidal hyperkinesias (84)	Mixed pyram./ extrapyram. c. p. (33)	Cerebellar ataxia and tremor (39)
Prenatal, anoxious	3	7	2	0	5½	1	*0*		
Prenatal, infectious	3	2	1	½	0	4	2		
Rh-incompatibility	2	1	0	0	0	0	*12*		
Prematurity (< 2500 g)	27	22	*50*	*44*	21	*16*	*14*	24	15
Birth weight > 4000 g	4	5	2	5	7	1	6		
Primary neonatal asphyxia	23	*31*	*12*	20	10	*4*	*42*	*52*	15
Birth trauma, undifferentiated	7	9	*1*	9	8	2	4		
Intracranial hemorrhage	2	2	3	½	3	4	0		
Secondary asphyxia	1	1	2	0	1	2	0		
Infantile, posttraumat.	4	1	1	0	*8*	*8*	0		
— , postinfectious	7	7	5	5	5½	9	10		
— , vascular accid.	3	0	0	0	3	*10*	2		
No factors elicitable	26	*18*	29	*19*	33	32	13	12	*39*

Total number of cases in each clinical subgroup is given on top.

some authors have placed some importance, was found only in 4 per cent, although slightly more frequent in right spastic hemiplegias (Table 1).

Practically the only information about postnatally acquired head injury and infantile vascular accidents was found in the case histories of our spastic hemiplegias. Again — in symmetric spastic diplegias — the incidence of birthtrauma as well as of neonatal asphyxia was surprisingly low.

The value of breaking down a statistic material in this way is illustrated convincingly by our figures on Rh-incompatibility, which is zero in all but two clinical subgroups: spastic tetraplegias — here found in 1 per cent only — and extrapyramidal c. p., where such a history was elicited in no less than 12 per cent (Table 1).

One of us (W.-N., 1953), after extraordinarily painstaking interviews with the parents to a minor part of our patients, found some statistical support to the opinion, that such factors as forceps delivery, multiple birth, induced labor and protracted labor are more common among our children with c.p., than among children in general. This was in accordance with findings made by Scheel-Thomsen (1953) on a small but carefully examined Danish group of unselected cerebral palsies.

We found in our present material multiple births in 7 per cent of our 163 spastic diplegias and i 7½ per cent of our 81 spastic tetraplegias, which is more than four times more frequent than normally. The general experience that congenital hydrocephalus is complicated with spastic diplegia is reflected in our figures, as this congenital abnormality was found in 4½ per cent of children belonging to this group, in contrast to barely 1½ per cent of the whole material.

Finally, it should be mentioned, because this factor seems to play a certain role in foreign statistics, that Caesarian section was never met with in any of 628 cases (our whole material) with cerebral palsy.

DISCUSSION

The fact that some degree of handicap — with the exception of very mild cases — will always persist in spite of modern treatment of cerebral palsy, makes it urgently important to look for preventive procedures. Without doubt the period of birth involves the most dangerous risk for brain lesion for all human beings. This in spite of the encouraging fact that the newborn baby is to some degree protected by special physiological mechanisms against damage caused by lack of oxygen, which is the ultimate cause of most lesions in the central nervous system. Therefore, most statistics based on follow-up studies of babies, asphyxiated at birth, give a rather optimistic impression. Campbell, Cheeseman & Kilpatrick in 1950 found only two athetoid children among 61 asphyxiated when examined 8—11 years after birth. In a study from the Mayo Clinic by Keith, Norval & Hunt, no evidence was found that prolonged labor, asphyxia er delayed respiration caused any neurological abnormality in newborn infants who survived, Fuldner in 1955, disagreeing with any generalization from this result, argues that extraordinarily good obstetrical service at the Mayo Clinic may account for the lack of neurological sequelae. Unfortunately this is an exception in most parts of the

world. Fuldner's own observations on 204 children with cerebral palsy, among whom at least 103 were anoxic at birth, is in good accordance with our findings — that lack of oxygen plays a dominating part in the etiology of cerebral palsy, and first of all in the types characterized by bilateral extrapyramidal or mixed pyramidal/extrapyramidal symptoms.

As pointed out by Fuldner, *duration* of anoxia is probably the all-determining factor deciding whether the newborn asphyxiated baby will escape cerebral damage or not. Findings by Eastman & Leon from Johns Hopkins Hospital are in agreement with this view at least. Twenty per cent of 96 cerebral palsied children did not respire until 120 seconds or more had passed after delivery and of these as many as 13 per cent waited for 6 minutes or even longer before they started to breathe. It is hoped that some reasons for protracted neonatal asphyxia may be eliminated through better obstetrics. Barbiturates and morphines, depressing the respiratory centers in the foetus, should be given only on special indications and not during the last few hours before birth. Abuse of pituitary extracts should be warned against. Prematurity has been blamed as predisposing to neonatal asphyxia, thus presenting a certain limit to prevention of asphyxia through obstetrical techniques. Our statistics offer no confirmation of this theory, since overlapping between prematurity and neonatal asphyxia was rather infrequent. The findings in Keith's series from the Mayo Clinic seems to offer an encouraging demonstration of what can be obtained through good obstetrics. As mentioned, Rh-incompatibility was found by us in 12 per cent of extrapyramidal cerebral palsy and neonatal asphyxia in 42 per cent. Prophylactic measures against these two factors will therefore reduce our most handicapping type of cerebral palsy up to 50 per cent.

Much more puzzling and obscure are the sources of premature birth. No denial can be given to the fact that most prematures develop quite normally and only a minor number will become spastic diplegias. Parasagittal hemorrhage from ruptured cortical veins during the accomodation of the cranial bones to the birth passage might be the complication explaining such a result. This should cause subdural hematomas in a certain percentage of newborn prematures. We do not know whether such bleedings have been sought for systematically in living newborn. We have been told that subdural punctures made on prematures showing abnormal neonatal behaviour, suspicious of some intracranial complication, will reveal no blood collections (Winge Flensborg, personal communication). This does not, however, exclude the fact that some local cortical disturbance to the cells of the motor area of the lower extremities might be caused from vascular congestion or minor perivascular bleedings. The relatively large percentage of spastic diplegias with unequal involvment of the lower extremities seems to favour a traumatic genesis in contrast to some early foetal damage, which should more likely cause a symmetric lesion.

Considerations like these may justify our hopes that lenient obstetric procedures may prevent, not merely some of the cerebral palsies caused by asphyxia, but also some of the spastic diplegias, most of whom showed no respiratory delay immediately after birth.

Finally, the possibility should be considered that mild but repeated — perhaps partially overlooked — hypoxia during neonatal life in some prematures may be responsible for damage to sensitive cells of the motor areas.

The role played by genetic factors in the etiology of cerebral palsy seems to be a minor one. The clinician will find that occasionally cases of degenerative progressive neurological disorders may be indistinguishable from stationary types of cerebral palsy for some years. In fact, suspicion about the malignant character of such cases is often unawakened until the familial nature of the disease is established through the onset of similar complaints in a younger sibling. In our clinic 26 such cases of familial neurological disorder have been diagnosed during the same period in which 628 cases of cerebral palsy were seen. This means a frequency of only 4 per cent.

Although we frankly admit that noxious factors of non-genetic nature operating during early pregnancy may be responsible for some cases of cerebral palsy, we do not find that our family histories offer us sufficient information to allow us to conclude that such factors play any important role in the etiology of cerebral palsy. Similar conclusions were made by Plum on his series of c. p. cases.

SUMMARY AND CONCLUSION

Obstetrical prophylaxis against neonatal asphyxia should be able to prevent up to 23 per cent of all cases of cerebral palsy. The gain may be even larger in respect to severely *handicapping* sequelae, because up to 50 per cent of the most serious clinical manifestations of the disorder (spastic tetraplegias, extrapyramidal and mixed extrapyramidal/pyramidal cerebral palsy) follow a history of perinatal anoxia. Procedures preventing premature birth or preventing complicating damage and anoxia to the parasagittal motor areas in the premature baby during and after birth will probably reduce our cases of spastic diplegias, among whom 44—50 per cent were premature, in contrast to 27 per cent of all cerebral palsied. The prophylaxis against cerebral palsy — so important in view of our rather limited therapeutic possibilities, which are primarily for the most disabling types — is a challenge to our obstetricians, who will probably be able to present

greater results in the future than other specialists studying the possibilities of preventing this disabling condition.

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ORTHOPEDIC SURGERY IN CEREBRAL PALSY

By J. MORTENS and H. MØLLER

The care of children with cerebral palsy at the Orthopedic Hospital in Copenhagen was improved in 1950 by the establishment of a teamwork between a neurologist (who is also a specialist in paediatrics), a doctor in physiotherapy and an orthopedic surgeon. We have analysed all cases operated on by the hospital's orthopedic surgeons between the beginning of 1950 and the beginning of 1957.

MATERIAL

One hundred and fourteen cases have been operated on. The clinic has seen 715 patients over the same period. Thus, the frequency of operation has been 16 per cent.

Spastics were operated on almost exclusively. 110 cases were spastics, 5 of these had additional ataxia and three atetosis. Only four cases were pure atetoids.

From Table 1 it will be seen that $^1/_3$ were hemiplegics. Three cases are included in this group because they had a monoplegia localised to the lower extremity. In $^2/_3$ of the cases our operative efforts were directed towards walking difficulties in children with tetra-, di- or paraplegia. In this group we have included the seven cases labelled as triplegia.

Table 1.
Localization.

	Number of cases	
Hemiplegia (right 22 + left 14)	36	39
Monoplegia	3	
Tetraplegia/Diplegia	46	
Paraplegia	22	75
Triplegia	7	
Total	114	114

The assessment of the *intelligence* will always involve some uncertainty. We have tried to divide the patients in three groups as shown in Table 2. If will be seen that only a little more than half the patients have been evaluated as having a normal intelligence.

Table 2.
Intelligence.

	Normal	Reduced slightly	Reduced severely	Total
Hemiplegia (Monoplegia) ..	24	15		39
Tetraplegia/Diplegia/ Paraplegia/(Triplegia)	38	20	17	75
Total	62	35	17	114

Preoperative treatment and age at operation.

As a rule we do not introduce surgery before the patient has been followed for several months during training by the team as well as by the physiotherapists. An exception to this rule has only been the comparatively small group which has come under treatment so late that sensible training would only be possible if structural contractures were abolished by operative interference. From Table 3, however, it is seen that almost $^1/_3$ have had no preoperative treatment. The reason is that facilities for physiotherapy at the hospital were first sufficiently built up for this group of patients during the year 1952. Some patients operated on in the first two years of the period have therefore been registered as having had no preoperative conservative treatment even though they might have had some, but then outside our control.

Table 3.
Preoperative treatment.

	Yes	No	Total
Hemiplegia (Monoplegia)	25	14	39
Tetra-Di-Paraplegia (Triplegia) ..	52	23	75
Total	77	37	114

Table 4 shows that 77 of the 114 cases have had preoperative conservative treatment. These 77 cases are grouped according to the age at start

From the Orthopedic Hospital, Copenhagen.

Table 4.
Age at start of conservative treatment on 77 cases.

Years	1	2	3	4	5	6	7	8	9	10	>10	Total
Hemiplegia (Monoplegia)	2	6	2	3		2	4	1	3	0	2	25
Tetra-Di-Paraplegia (Triplegia)	5	5	6	5	4	6	1	5	3	2	10	52
Total	7	11	8	8	4	8	5	6	6	2	12	77

Age at operation on preoperatively treated 77 cases.

Hemiplegia (Monoplegia)				1	3	3	3	3		2	10	25
Tetra-Di-Paraplegia (Triplegia)			3	2	6	4	3	3	4	4	23	52
Total			3	3	9	7	6	6	4	6	33	77

Table 5.
Years from onset of treatment to operation on 77 cases.

Years	1	2	3	4	5	6	7	8	9	10	>10	Total
Hemiplegia (Monoplegia)	3	3	6	4	3	1	1	1	1		2	25
Tetra-Di-Paraplegia (Triplegia)	9	10	10	8	6	3	3	1	1		1	52
Total	12	13	16	12	9	4	4	2	2		3	77

Table 6.
Age at operation on 37 cases with no preoperative treatment.

Years	1	2	3	4	5	6	7	8	9	10	>10	Total
Hemiplegia (Monoplegia)						2	1	1	2		8	14
Tetra-Di-Paraplegia (Triplegia)		1	1	2	1	3	1	1	2	2	9	23
Total		1	1	2	1	5	2	2	4	2	17	37

of the conservative treatment and the age at operation. It will be seen that many of the patients whom we thought might benefit from an operation came under conservative treatment at a very young age. However, only few were operated on under five years of age. Half the patients were operated on between the age of five to ten. Less than half the patients after ten years of age.

According to this many patients have had a long preoperative treatment (Table 5). One third have had five years or more before operation. The greater part, however, were operated on after shorter period of treatment.

In Table 6 the 37 patients who had no preoperative treatment are grouped according to age at operation. The distribution of cases in the different age groups is fairly similar to that presented in Table 4 for the preoperatively treated cases.

It will be seen that operations have been performed earlier in tetra- di- and paraplegic patients than in hemiplegic patients. We have been inclined to operate on some severely handicapped children with tetraplegia, who were not able to walk or walked very badly in spite of adequate training, in the hope of improving their walking ability. In the hemiplegic children we have postponed operations to a somewhat later age as these patients were able to walk in spite of an equinus foot.

Most of the patients have been operated on at the age of five or later with a fairly even distribution in the different age groups. Some adults are included in the group older than ten years.

TYPES OF OPERATION

The aim of operation on these children with spastic cerebral palsy is to restore or improve muscle balance, proper alignment of joints, and establishment of correct posture with normal relationship to the line of gravity. The usual well known orthopedic interferences have been employed. Myo-tenotomies or tendon lengthenings and stabilising procedures to obliterate joint movement or correct joint deformities have been preferred. However, in some instances neurectomies have been done, but then always as a partial denervation of a muscle group. Most often it has been to reduce adductor spasm. Partial denervation to the calf muscles has only been done in cases where severe clonus was present and its use has gradually decreased during the time. Capsulotomies have been necessary in some cases with old structural deformities. Only a single osteotomy is present in the analysis, but we now

employ it to some extent in order to improve alignment.

In Tables 7 operations carried out upon hemiplegics are grouped for the lower and upper extremities. In these tables as well as in the following tables the actual numbers of procedures performed are summarized. By an "individual operation" is therefore understood an interference on a single muscle or joint function and localisation.

Table 7.
Individual operations on 39 patients with hemiplegia (monoplegia).

	Number of operations
Lower Extremity: 36 patients.	
A. Neurectomies	
on triceps surae	3
B. Myo-tenotomies	
on gastrocnemii (Silfverskiöld)	3
— tibialis posterior	1
— plantar fascia (Steindler)	2
C. Tendon lengthenings	
Achilles tendon	26
D. Tendon transplantations	
tibialis anterior	2
E. Stabilizing/corrective bone operations	
Triple arthrodesis of foot	7
Upper Extremity: 6 patients.	
B. Myo-tenotomies	
on pronator quadratus	6
— wrist flexors	3
D. Tendon transplantations	
pronator teres	2
wrist flexors	3
E. Stabilizing/corrective bone operations	
wrist arthrodesis	4

Table 8.
Individual operations on 75 patients with tetra-di-paraplegia (triplegia).

	Number of operations
A. Neurectomies	
on hip adductors	20
— triceps surae	18
B. Myo-tenotomies	
on hip adductors	34
— — flexors	23
— — inwards rotators	17
— ileo-tibial band at knee (Yount)	7
— gastrocnemii at knee (Silfverskiöld)	30
— tibialis posterior	1
C. Tendon lengthenings	
Hamstrings	31
Achilles tendon	34
Tibialis posterior	1
D. Tendon transplantations	
tibialis anterior	3
— posterior	2
Peronæus longus	2
— brevis	1
Extensor hallucis longus	2
Part of hamstrings to patella	2
Retransplantation of hamstrings	1
E. Stabilizing/corrective bone operations	
Triple arthrodesis of foot	10
Grice's extra-articular arthrodesis of foot	10
Arthrodesis of hip	1
Osteotomy of femur (Schantz)	1
Reduction of hip	1
F. Various.	
Capsulotomy of hip	2
Capsulotomy of knee	9
Total	325

Achilles tendon lengthening has been done on 26 of the 39 patients with hemiplegia, and arthrodesis of the foot in seven cases. The Silfverskiöld operation of myo-tenotomy of the gastrocnemii at the knee joint has been performed only in three instances of hemiplegia, but it is a procedure which is often used in the paraplegic type of spastics.

In only four of the 39 patients with hemiplegia we have felt inclined to try to improve hand deformity and function by arthrodesis of the wrist joint with or without tendon transplantations. In two cases interference at muscles and tendons alone has been done in order to reduce pronation deformity of the forearm, secondarily to reduce flexion deformity of the wrist and improve abduction of the thumb.

In Table 8 the 263 "individual operations" on the 75 patients with tetra-di-paraplegia are presented. The figures in group B and C show that myo-tenotomies or tendon lengthenings have been done with almost the same frequency at the hip, knee and ankle joint. Concerning group E, stabilising procedures of the foot have either been done as an ordinary triple arthrodesis on patients of age twelve and over or as the operation designed by Grice for the paralytic valgus foot on younger children, down to the age of five.

In all, 325 "individual operations" have been performed on the 114 patients.

Frequency of single or combined operations.

We have grouped the patients in three groups according to whether they have had an "individual operation", a "combined operation" or "several combined operations".

Thirty-four patients had only an "individual operation". Fifty-four patients had a "combined operation". That is, several individual operations performed with a few weeks' interval or at the same time, often as a bilateral procedure, less often bilateral on more than one joint. Twenty-six patients had several "combined operations" with months' or years' interval. The rule has been to follow the operated child during the postoperative training before further procedures in a planned program were performed. In some cases however, in the group of the 26 patients the interference already carried out was felt inadequate during the following training, and therefore more surgery was felt necessary.

On an average two to three operations were

done on each patient. (It should perhaps be mentioned that in twenty-six of the 114 patients concerned 90 individual operations had already been done before the patients came to the cerebral palsy clinic, but these operations are not included in the analysis).

RESULTS

The follow-up is brief in this analysis. For those children operated upon at an early age the results presented must be regarded with some reservation, even if the follow-up is several years. What seems to be gained by an operation might be lost again during the further growth of the patient. In spite of continued training the child might fall back into the bad walking pattern it had before operation. For those operated in late childhood or in adolescence the results are more reliable. The cases are too few to warrant an analysis as to age and length of observation period, and the results presented are therefore only to be regarded as preliminary. However, we have felt it necessary to estimate these preliminary results, as our physiotherapists ask for operative help more often than was the case when we opened our clinic and established the new facilities for these children with cerebral palsy to have thorough physiotherapy and training. We also wished to see, if possible, whether the interferences we had selected among the many different operations possible were the best, or other types should be introduced.

In our assessment of results we have endeavoured to be strict. We have especially tried as far as it is possible not to claim an improvement as due to the operation done if the training or the growth and mental development of the child with reason could be said to be responsible for the improvement. Films at intervals before operation and after, the estimation from the other doctors in the team and from the physiotherapist responsible for the treatment before and after operation have been very helpful in this respect. And where there has been any doubt we have rated the result of operation as doubtful.

Results of operations on the upper extremity.

Table 9 shows the results on the few cases we have operated on for pronation and flexion deformity of the arm and hand. We have obtained improvement of function on three of the six cases. In one of the cases, however, where only tendon-transplantations were done, the improvement was very slight. In two cases the improvement was only cosmetic.

Results of operation on the lower extremity.

In Table 10 the first group concerns those cases where the preoperative condition as to walking ability was such that walking was impossible, or only possible in an awkward way with the help of a person or in walking bars, in spite of long training. The operation done has made it possible for the seven children in this group to walk in the following way: five without any support whatsoever, two with elbow crutches. Naturally, there are no hemiplegics in this group as these children could walk before operation.

Table 9.
Upper extremity.
Results on 6 patients.

	Hemiplegia (monoplegia)	Total
Function of hand *improved*	2 wrist arthrodesis ± tendon transpl. 1 tendon transpl.	3
Cosmetic improvement	1 wrist arthrodesis 1 tendon transpl.	2
Too early for assessment	1 wrist arthrodesis + tendon transpl.	1
	Total....	6

Table 10.
Lower extremity.
Results on 111 patients.

	Hemiplegia (monoplegia)	Tetra-di-paraplegia (triplegia)	Total
Operations *decisive* for walking ability		7	7
Operations have *improved* walking ability	32	42	74
Operations have *possibly* improved walking ability ..	3	18	21
Operations have *not* improved walking ability ..	1	8	9
Total	36	75	111

Only seven cases come into this best group. By far the most cases come into the next group: "improved walking ability". All the hemiplegics except the few with recurrence of the tight achilles tendon fall into this group, but also 42 of 75 children with tetra-, di- or paraplegia. Most of these children can walk about with less support than before operation. However, a few patients are included who before operation could only walk in the walking bars or not even walk at all. These patients can now move about more freely in the walking bars and with a better posture. There is a fair prospect of these children being able to walk outside the bars as a final result.

There are 26 patients with tetra-, di- or paraplegia in the two last groups where no certain improvement has taken place. Six of these cases, however, are operated so recently that evaluation is impossible.

The degrees of spasticity and contractures as well as the age groups at operation are fairly evenly represented in all four groups of assessment. We do not feel that these factors are de-

Table 11.
Localisation of interference on the lower extremity on 111 patients — in the different groups of results.

	Hemiplegia (monoplegia) 36 patients	Tetra-di-paraplegia (triplegia) 75 patients
A		
Operations *decisive* for walking ability 7 patients		
Foot		2
Knee		3
Hip		
Mixed		2
Total		7
B		
Operations have *improved* walking ability 74 patients		
Foot	29	11
Knee	3	11
Hip		6
Mixed		14
Total	32	42
C		
Operations have *possibly* improved walking ability 21 patients		
Foot	3	4
Knee		4
Hip		4
Mixed		6
Total	3	18
D		
Operations have *not* improved walking ability 9 patients		
Foot	1	1
Knee		1
Hip		4
Mixed		2
Total	1	8

Table 12.
Reasons for uncertain results or no improvement on 21 + 9 = 30 patients.

6 cases:	Operations done too recently for assessment.
7 cases:	Probably unaltered; interference perhaps not sufficient.
1 case:	Progressive brain affection.
4 cases:	Atetosis — no certain improvement.
1 case:	Reoperated to minimise sequels of earlier operations — with no certain effect on walking ability (but in other respects improved).
1 case:	Hip reduction at age of 2 years; can still not walk at age of five.
4 cases:	Myo-tenotomies on hips have reduced inward rotation, flexion deformity but probably produced some instability (positive Trendelenborg).
3 cases:	Total/subtotal recurrences of Achilles tendon contracture after tendon lengthening.
1 case:	Combined neurectomy to triceps and Achilles tendon lengthening have produced slight calcaneus deformity.
2 cases:	Persistence of knee hyperextension in spite of myo-tenotomy on gastrocnemii.

cisive for the possibility of improvement by operation.

The analysis has not given any definite clue to the important question of what "localisation" is the best to tackle by our corrective operative measures. In Table 11 we have tried to illustrate this opinion. Operations on the hip, the knee and the ankle or foot are represented with fairly even frequencies. In these cases of tetra-, di- or paraplegia with flexed, adducted and internally rotated hips, with bent knees in valgus and the feet in equino-plano-valgus positions, it can be very difficult to decide what "localisation" should first be corrected by operation. But fortunately, if a correction takes place in one joint it also benefits the other misalignments of joints with improved posture as a result.

Finally in Table 12 we have summarized those cases where operations have not given any certain effect.

DISCUSSION

We feel that several patients were greatly improved by the operation done, so far as training has been facilitated and posture and gait improved. In many of the patients, however, the results have not been so conspicuous and only little has been gained. But in these children with cerebral palsy with a very severe motor handicap even a slight improvement warrants in our opinion the operative efforts. It is perhaps worth while to state that we do not feel — perhaps with one exception — that operation has made conditions worse. Temporarily, there can be a relapse or stand-still in progress when training is resumed after weeks or months of immobilisation of operated limbs. It can be necessary to tell relatives and physiotherapists that the relapse will soon be overcome by further training, in order to reassure them. We personally believe that this seemingly negative response to surgery mainly was responsible for the bad reputation surgery fell into in pre-war years, when children were discharged from the orthopedic hospitals without being started on a proper post-operative treatment program.

There should be no deterioration by operation if operations are only instituted after careful observation during treatment, if one keeps to the types of operation where results are best predictable, *i. e.*, myo-tenotomies, tendon lengthenings and joint fusions, and if one reduces the employment of the less predictable procedures such as tendon transplantations and neurectomies. If operations are followed by adequate splinting and skilled training and if only one operation or one combined operation is done at the time and the result observed during postoperative training before the next step in the operation program is taken, then there should be no further risk than that the operative efforts might turn out to be an insignificant help in the training program.

The trend in modern literature shows a revival of orthopedic surgery in treatment of cerebral palsy. It is realised that operative interference can be helpful in the training program. Many of the difficult tasks encountered in the rehabilita-

tion of the children with cerebral palsy can be carried out more readily following surgical improvement of muscle balance and corrections of deformities. Our operative frequency is similar to that encountered in the literature over the later years.

Even though the gain by surgery in cerebral palsy is often distressingly small, properly selected procedures to minimise uncontrolled spasticity or tension which interfere with the restoration or improvement of ambulation — with or without crutches or braces — should be carried out.

We do not have much experience in deformities of the arm, wrist, and fingers. The opinion expressed in modern literature is not encouraging, and the frequency in the literature of operation upon the upper extremity is not greater than ours. Cosmetic improvement can often be obtained by a wrist arthrodesis combined with myo-tenotomies and tendon transplantations. But only occasionally is there a significant improvement of function. In our opinion one should never let the patient or his relatives expect more from a planned operation than improvement of the look of the hand and arm with a chance of a minor improvement of function. A recent publication by Goldner is somewhat more optimistic. It might be worth while also to use finger and thumb arthrodesis and enlarge the field of selective muscle transplantations to the finger tendons in the effort to open up the hand for grasp and pinch and convert it from a tool of support only to a tool of somewhat more usefulness.

Most of our operative efforts have been directed towards improving walking ability in children with moderate and severe tetra-, di- or paraplegia. Two important questions concerning the possibilities of operations in such severely handicapped children have to be answered: How early in the training program should one operate to obtain maximum benefit from the correction? And which of the many possible interferences are the best remedies for the multiple and many-sided deformities one is confronted with in each individual case? These questions are to our mind not convincingly answered in the large literature available. Phelps in his latest contribution to the question expresses the opinion that the best results are obtained by late interferences and that corrective measures on bone and joints give the best results. Baker states that surgery if indicated should be carried out early in the rehabilitation program in order to reduce the difficulties for the physiotherapist in his work. He advocates mainly operations upon muscles and tendons.

The present analysis cannot answer these questions. However, the analysis and our experience over seven years also with training of spastics not operated upon has led us to formulate an opinion — stated below — for our future attitude towards the role of orthopedic surgery in the rehabilitation of children with spastic tetra-, di- or paraplegia. An attitude which we are well aware might prove correct only on analysis after more years of experience.

We feel it is worth while in many cases to operate early in order to establish a better walking pattern during further training or to enable a child to walk independently of a walking bar and to minimise or prevent progression of deformities. Such early interferences we would direct towards correction of knee flexion deformities and equino-plano-valgus deformities of the feet. The remedies we find useful for these purposes are tendon lengthening of the hamstring muscles and myotenetomies of the gastrocnemii or a moderate lengthening of the Achilles tendon. Also stabilizing of the foot by the Grice extra-articular subtaloid arthrodesis in selected cases.

The two operations described by Eggers: The transcision of the patellar retinacula and the reinsertion of the hamstrings to the popliteal plane of the femur to minimise knee flexion deformity we have found helpful during the last year; also the advancement of the patellar tendon distal on the tibia to place the patella in a more normal relationship to the femur in selected cases.

We feel that surgical correction of internal rotation, flexion and adduction deformity of the hip is best done at a later age by a derotational osteotomy on the femur. The deformity should of course be rather severe to warrant such a procedure, but especially in girls the deformity can be very unsightly. This does not mean that we do not think there occasionally is a place for earlier operation on the hip, but myo-tenomities of hip flexors and internal rotators do not seem to correct the deformity very much and there is a risk of producing an insufficiency of the hip abductors. Tenotomy of the adductors and partial neurectomy to the adductor muscles at a younger age is indicated when it is felt that the scissoring of the legs is the main obstruction to improvement of ambulation.

We might add that apart from this partial neurectomy on the obturator nerve we seldom find this type of operation indicated; however, occasionally partial neurectomy to the calf muscle can be helpful when severe clonus of the foot in a child with the "extensor thrust" type of deformity prevents ambulation, in spite of a previous lengthening of the muscle-tendon apparatus.

It is almost exclusively in the spastic type of cerebral palsy that orthopedic operations are indicated. However, we feel that sometimes a dystonic child with so-called "rotatory atetosis" of the ankle and foot can benefit from a subtaloid arthrodesis — in the younger age performed after the manner of Grice. These children often have a very soft foot which on weight-bearing collapses in severe planus; also for this reason can such an operation be indicated.

SUMMARY

The results are presented of various orthopedic operations on 114 children with cerebral palsy from the clinic for cerebral palsy at the Orthopedic Hospital, Copenhagen. Most of the children were spastics; they were operated on during the years 1950 to 1957. The frequency of operation was 16 per cent. The results in most cases were good, even though only slight improvement was obtained in several of the cases, and no improvement at all in some. A program for our future attitude towards the role of orthopedic surgery in the rehabilitation of children with cerebral palsy is outlined.

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THE PROGNOSIS IN CEREBRAL PALSY

By P. PLUM

Everyone who has worked with cerebral palsy knows how difficult it is to establish the prognosis and how difficult it is to evaluate the effect of treatment. The present account may be interpreted as an investigation of the extent to which a review of a limited material of patients can contribute to the solution of the question.

The investigation was undertaken in such a manner that each case history was reviewed in respect of the most important clinical criteria: The nature of the paresis, the degree of motor handicap, the degree of intelligence defect, if any, and degree of speech defect, if any, as these symptoms presented themselves at the commencement of treatment. The case histories were then reviewed as regards the course within the period of observation in respect of motor and intellectual development and the development of speech. Finally, an attempt was made to estimate whether the treatment was carried out satisfactorily or not. The relations between the various symptoms and combinations of symptoms on the one hand and the course on the other hand and finally between the intensity of the treatment and the course, were investigated.

MATERIAL

The limited number of the patients, total 203, is balanced, to some extent, by the fact that each patient was examined by the same physician several times annually, as a rule throughout the entire period of observation. The case histories were supplemented by films once or twice annually where the majority of patients are concerned. The material comprizes all definite cases of non-progressive cerebral palsy who have been under observation in our clinic for three years or more (Table 1). In the majority of cases the patients were treated throughout the entire period of observation, but in isolated cases the period of treatment was shorter than the period of observation, but in no case was this less than three years. Out of the 230 patients observed for more than three years 21 were excluded on account of uncertainty in the diagnosis and six on account of the progressive nature of the disease. The 203 patients included in the material constitute slightly more than a third of the total number of patients attending the clinic, *viz.*, 590.

Table 1.
Period of observation.

Years	No. cases
3 0/12— 4 11/12	92
5 0/12— 6 11/12	82
7 0/12— 8 11/12	18
9 0/12—13 11/12	11
Total	203

To investigate whether the criterion of a period of observation of at least 3 years might imply a selection of slighter or more severe cases, the incidence of intelligence defect in the total material of cerebral parasis of our clinic over the age of 4 years is compared with the corresponding figure in the material employed. As in both groups 34 per cent of defective intelligence was found, it seems reasonable to presume that no great difference is present.

DEFINITIONS

If an investigation such as this is to be compared with other investigations it is necessary that the criteria for subdivision be defined. As the clinical diagnoses may be interpreted differently, a brief account of what is understood by our diagnoses must be given.

By spastic hemiplegia is understood cases of pure hemiplegia; if the opposite limbs are also affected the diagnosis of tetraplegia is employed

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even when the spastic paresis is much more pronounced on the one side.

By spastic paraplegia is understood cases in which the lower limbs only are affected to such an extent that it is of practical significance; cases in which the symptoms from the upper limbs are quite insignificant are thus classified as cases of paraplegia and not as cases of tetraplegia or diplegia. In an isolated case only, which developed following meningitis, the upper limbs were affected while the lower limbs were normal.

By tetraplegia is understood cases where all 4 limbs are definitely affected, irrespective of whether the affection is symmetrical or asymmetrical and whether the upper or lower limbs are most affected. If the diagnosis of diplegia had been employed, eight of the cases of paraplegia and 21 of the cases of tetraplegia would have been classified in this group.

By athetosis is understood cases which are characterized by involuntary uncontrollable movements and by greatly varying muscle tone without contractures and without greatly increased tendon reflexes.

Under ataxia are included such cases of cerebral paresis which, without exhibiting spasticity or athetosis, are characterized by poor balance and poor muscular coordination.

The motor handicap and the degree of speech defect are subdivided into slight, marked and severe and the intelligence is classified as normal, somewhat retarted and greatly retarded.

By slight motor handicap is understood a handicap which does not prevent the patient from carrying out the movements necessary in daily life.

Cases are classified as possessing marked motor handicap in which a defect of movement renders it impossible to carry out the ordinary movements in a normal manner and in which the carrying out of these movements demands considerable exertion.

Severe motor handicap indicates a handicap which, practically speaking, completely prevents the patient from carrying out voluntary movements with the parts of the body involved.

In estimating the intelligence, only slight emphasis has been placed on the result of intelligence tests, which, in our experience, are not infrequently misleading in cases of cerebral palsy. The intelligence is estimated by conversations with the parents several times annually and by repeated observations of the child; thus a patient, observed throughout 4 years, would be observed by the author on an average, 12—16 times, for an hour on each occasion. The impression thus obtained is supplemented and corrected by accounts from the physiotherapists, nurses, nursery school teachers, occupational therapists, schools, etc.

A patient is classified as of normal intelligence when it is estimated or known that he can fulfil the requirements of a normal school or would be able to do so, had it not been for the physical handicap.

By moderately retarded intelligence is meant an intelligence defect which permits a certain education not, however, in a normal school.

By greatly retarded intelligence is understood oligophrenia of such an extent that education and vocational training are impossible, at any rate from a practical viewpoint.

By slight defects of speech are understood such defects which do not, to any great extent, prevent the patient from speaking understandably.

As marked speech defects are classified speech defects, which seen from a practical viewpoint, completely prevent the patient from speaking.

By satisfactory progress as regards motor, intellectual or speech development is understood progress which approximates the patient to normal in this respect. By some progress is meant progress which is undoubted but which is not satisfactory and which is not sufficient to ap-

Table 2.
Age at first examination.

Age at first examination	No. cases					
	Hemiplegia	Paraplegia	Tetraplegia	Athetosis	Ataxia	Total
0—30 days	3	0	5	3	0	11
1— 5 months	0	0	3	1	0	4
6—11 months	4	1	5	2	0	12
12—17 months	6	3	12	8	1	30
18—23 months	7	4	11	5	0	27
2 0/12— 2 11/12 years	5	10	8	7	3	33
3 0/12— 4 11/12 years	6	10	9	6	3	34
5 0/12— 6 11/12 years	8	5	8	2	0	23
7 0/12— 8 11/12 years	2	2	5	0	0	9
9 0/12—10 11/12 years	2	0	2	0	0	4
11 0/12—12 11/12 years	2	2	2	0	1	7
13 0/12—14 11/12 years	1	3	0	0	0	4
15 years and over	3	0	2	0	0	5
Total	49	40	72	34	8	203

proximate the patient to normal to any great extent. By no progress is understood no progress at all or such slight progress that it is of no practical significance. The few cases which have shown regression are classified in this group.

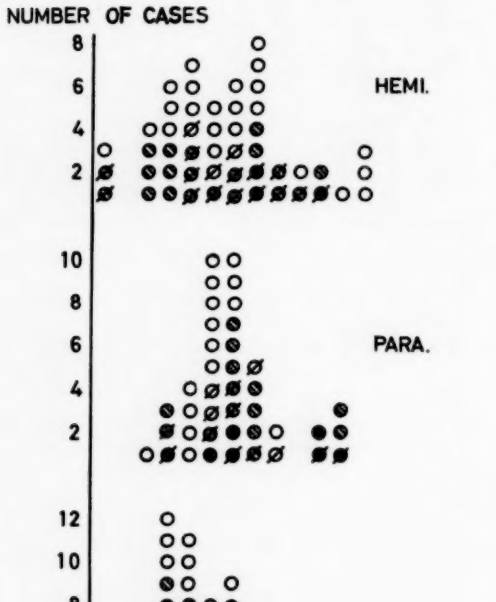

Fig. 1.
Age at commencement of treatment compared with results obtained and with intensity of treatment.

SYMPTOMS

The distribution of the patients as regards the diagnoses and the age at the first examination appears from Table 2 and Figure 1, and the distribution as regards the degree of severity of affection of motor development, intelligence and speech from Figure 2 and Table 3.

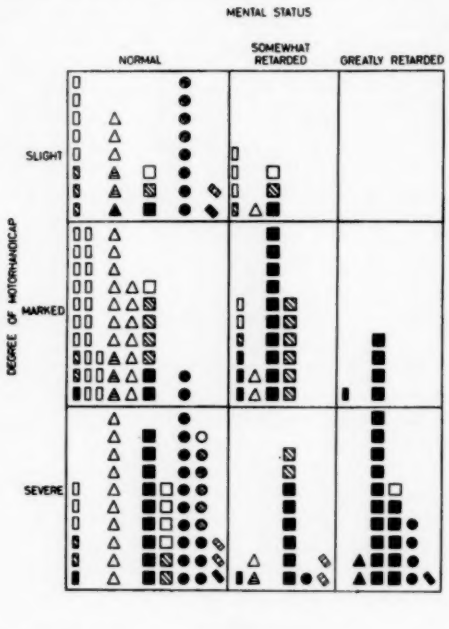

Fig. 2.
Relation between the diagnosis, mental status, degree of motor handicap and impairment of speech.

Table 3.
The percentage distribution of the various degrees of severity of affection of motor development, intelligence and speech. For details see Figure 2.

Slight motor handicap	17 per cent
Marked motor handicap	38 per cent
Severe motor handicap	44 per cent
Total	100 per cent
Intelligence normal	63 per cent
Intelligence moderately retarded	23 per cent
Intelligence greatly retarded	14 per cent
Total	100 per cent
Speech normal	36 per cent
Slight defects of speech	22 per cent
Marked defects of speech	42 per cent
Total	100 per cent

Table 4.
Distribution of the patients as regards the necessity of speech therapy.

		Hemiplegia	Paraplegia	Tetraplegia	Athetosis	Ataxia	Total
Speech therapy not prescribed		43	38	20	9	4	114
Ditto on account of intelligence defect		2	2	20	2	1	27
Speech therapy prescribed	Undergoing therapy	3	0	7	3	0	13
	Not commenced	0	0	16	15	3	34
	Concluded and now not required	1	0	1	1	0	3
	Attempted but abandoned	0	0	3	0	0	3
	Desirable but child not old enough	0	0	5	4	0	9
		49	40	72	34	8	203

TREATMENT

Speech therapy, school attendance, care under the Mental Deficiency Act.

The treatment comprized exercises, mainly in the form of treatment in the home, carried out by the parents according to the author's instructions; treatment with bandages, splints and plaster of Paris; treatment with apparatuses, such as "crawlers", "walkers", tricycles etc.; primitive speech therapy; medical treatment (particularly mysoline in athetosis, 5 mg per kg body weight per 24 hours); if possible, attendance at a nursery school.

In 25 cases operative orthopaedic therapy was employed, in ten cases prior to treatment in our clinic and in 15 cases during treatment here. The latter 15 children were operated upon within the past year, and it is therefore not yet possible to evaluate the results. Where these 15 children are concerned the result of treatment was evaluated until the period immediately prior to operation.

Actual speech therapy was undertaken to a much lesser extent than required. As appears from Table 4 speech therapy was considered unnecessary in 150 cases and to be necessary in 53 cases. Only 19 out of these 53 patients actually received such therapy.

Out of the 124 children of school age (over 7 years) 76 were of normal intelligence, 35 somewhat retarded and 13 greatly retarded. It will be seen from Table 5 that approximately 10 per cent of the children with normal intelligence received no education while 30 per cent of the somewhat retarded and all of the greatly retarded patients received no education.

No less than 53 out of the 76 children with normal intelligence (70 per cent) attended normal schools. The distribution as regards the school attendance in the individual diagnostic groups is seen from Figure 3.

Two patients with hemiplegia, 17 with tetraplegia, five with athetosis and one with ataxia, a total of 25 out of 203 (12 per cent) were under the care of the Mental Deficiency Act. Out of the 124 children of school age 16 (13 per cent) were under the care to the Mental Deficiency Act.

Table 5.
Education of 124 children with cerebral palsy of school age.

Degree of motor handicap	Normal school	Education elsewhere	No education	Total
Normal intelligence.				
Slight	13	3 (School for deaf 2)	0	16
Marked	26	0	2	28
Severe	14	13 (Orthopaedic hospital 4 At home 8)	5	32
Total	53	16	7	76
Somewhat Retarded Mentally.				
Slight	1	9 (At home 8)	1	11
Marked	2	10 (Orthopaedic hospital 3 At home 6)	6	18
Severe	2	1	3	6
Total	5	20	10	35
Greatly retarded mentally.				
Slight	0	0	1	1
Marked	0	0	4	4
Severe	0	0	8	8
Total	0	0	13	13

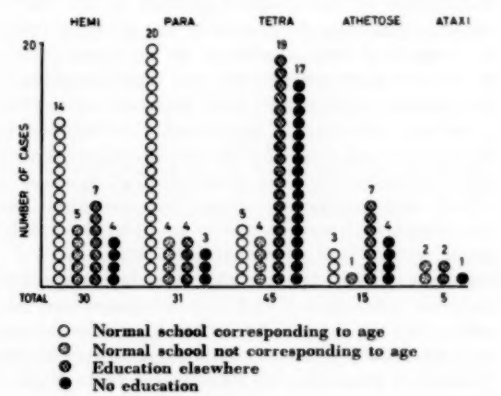

Fig. 3.
School attendance, 126 children with cerebral palsy over the age of 7 years.

Table 6.
Progress as regards motor ability intelligence and speech in the various diagnostic groups.

	Hemiplegia	Paraplegia	Tetraplegia	Athetosis	Ataxia	Total
Satisfactory motor progress	26	19	18	14	2	79
Some motor progress	20	14	31	17	4	86
No motor progress	3	7	23	3	2	38
Total	49	40	72	34	8	203
Satisfactory intellectual progress	37	36	24	28	5	130
Some intellectual progress	12	4	32	4	2	54
No intellectual progress	0	0	16	2	1	19
Total	49	40	72	34	8	203
Satisfactory progress in speech	44	38	27	17	2	128
Some progress in speech	4	2	21	9	6	42
No progress in speech	1	0	24	8	0	33
Total	49	40	72	34	8	203

COURSE AND PROGNOSIS

Using the criteria mentioned above the relationship between the diagnosis, degree of handicap and complications on the one hand and the course of the disease, on the other hand, was investigated. As a whole, the group of patients investigated showed definite progress. As appears from Table 6 satisfactory motor progress occurred in a total of 39 per cent of the cases, satisfactory intellectual development in 64 per cent and satisfactory development of speech in 63 per cent of the cases.

Motor progress was best in the group of patients with hemiplegia where 53 per cent of the patients showed satisfactory progress, and progress in mental and speech development was best in the group of patients with paraplegia where 90 per cent and 95 per cent, respectively, showed satisfactory progress.

In order to establish the prognosis in an individual case it is necessary to know the relationship between the diagnosis, the degree of the single handicaps and the course of the disease. It will be observed from Figures 4, 5 and 6 that the degree of the single handicap is the factor which influences the course to the greatest extent in respect of this handicap. In addition it will be observed, as anticipated and corresponding to the general impression, that progress as regards a certain handicap is unfavorably influenced by the presence of severe handicaps elsewhere. Favorable prospects are thus much greater in cases in which slight motor handicap is present alone, not associated with speech defect or defective intelligence.

As demonstrated previously, there is a connection between intelligence and certain symptoms, *viz.*, subnormal circumference of the head, strabismus and seizures (epilepsy). This relationship is also present in this material as appears from Table 7 and Figure 7. It seems reasonable to assume that correlation between normal intelligence and these symptoms is different within the diagnostic subgroups, in other words that *e. g.*, the presence of epilepsy might be of more serious prognostic significance as regards intelligence in *e. g.*, tetraplegia than in hemiplegia. An investigation of this possibility showed that the conditions were as in the example given above. Out of the 16 patients with tetraplegia and epilepsy none had normal intelligence while 45 per cent of the 56 patients with tetraplegia and no epilepsy had normal intelligence. The corresponding figures for hemi-

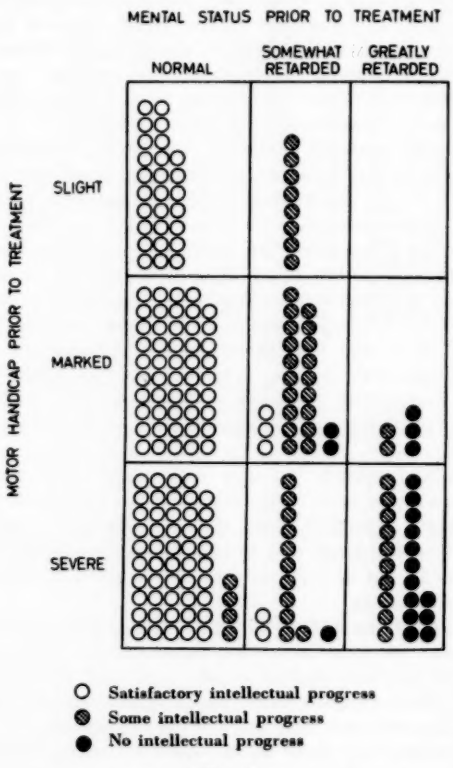

Fig. 4.
Mental development during treatment.

Table 7.

Correlation between presence of normal intelligence and occurrence of certain symptoms within the various diagnostic groups of cerebral palsy.

	Hemiplegia	of these with normal intelligence		Paraplegia	of these with normal intelligence		Tetraplegia	of these with normal intelligence		Athetosis	of these with normal intelligence		Ataxia	of these with normal intelligence		Total	of these with normal intelligence	
	No.	No.	per cent	No.	No.	per cent	No.	No.	per cent	No.	No.	per cent	No.	No.	No.	No.	per cent
Epilepsy	16	9	56	1	0	—	16	0	0	1	1	—	1	0	35	10	29
No epilepsy	33	28	85	39	33	85	56	25	45	33	28	85	7	5	168	119	70
Total	49	37		40	33		72	25		34	29		8	5	203	129	
Microcephaly	5	2	—	2	2	—	23	3	13	5	3	—	1	0	36	10	28
No microcephaly*)	38	30	79	32	25	78	39	16	41	25	22	88	7	5	141	98	70
Total	43	32		34	27		62	19		30	25		8	5	177	108	
Strabismus	14	10	71	15	11	73	40	13	33	14	11	78	3	2	86	47	55
No strabismus ..	35	27	77	25	22	88	32	12	38	20	18	90	5	3	117	82	70
Total	49	37		40	33		72	25		34	29		8	5	203	129	

*) Circumference of head from — 2.4 to + 2.4 cm from average.

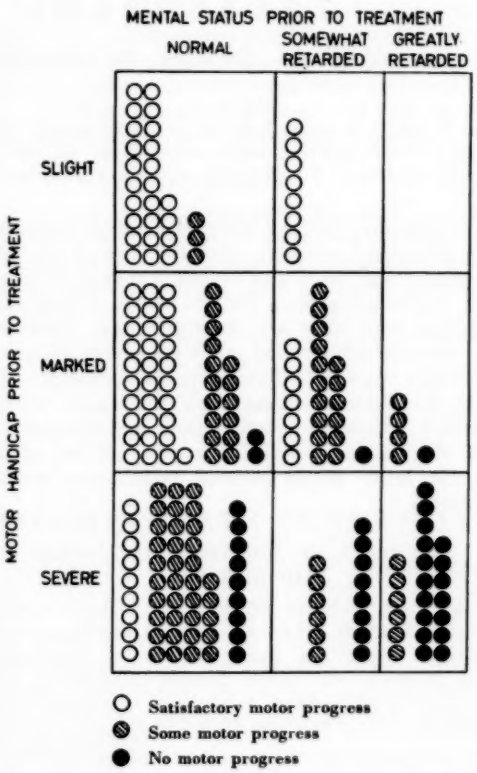

Fig. 5.

Result of treatment of the motor handicap in relation to the mental and motor status prior to treatment. 203 patients.

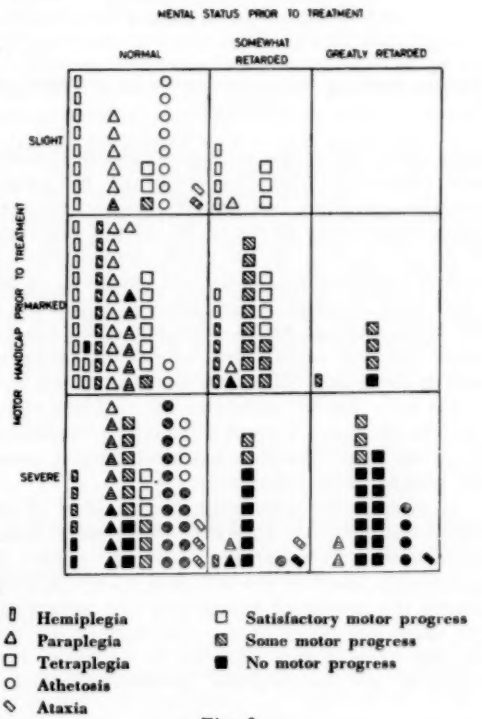

Fig. 6.

Result of treatment of the motor handicap in relation to the diagnosis, mental status and motor status prior to treatment. 203 patients.

plegia were 56 per cent and 85 per cent, respectively. Corresponding observations exist for subnormal circumference of the head although the figures are small in the individual groups.

As a connection has been shown to exist between intelligence and the course of the disease, a similar connection might be anticipated in advance between the circumference of the head and the course of the disease. If the upper limit of microcephaly is regarded as 2.5 cm less than average (the normal curve was constructed on a basis of measurements in 100 normal children and the available published normal values for boys and girls), it appeared that, in respect of motor progress, there was no demonstrable differ-

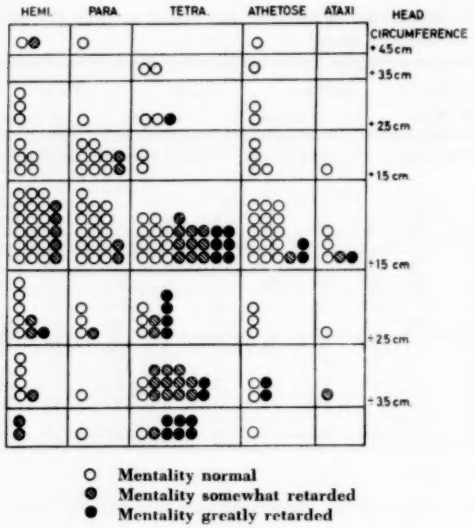

Fig. 7.
Relation between the circumference of the head and intelligence.

ence when the group of microcephalic children was compared with the group of non-microcephalic children, satisfactory motor progress being observed in 12 out of 36 (33 per cent) and in 53 out of 141 (38 per cent), respectively. As regards satisfactory intellectual progress, on the other hand, a great difference was observed: in the microcephalic group, nine out of 36 (25 per cent) showed satisfactory intellectual progress and in the group with circumference of the head + 2.4 to ÷ 2.4 cm inclusive, 100 children out of 141 (71 per cent) showed satisfactory intellectual progress. This difference was most marked among the patients with tetraplegia.

As regards the prognostic significance of seizures (symptomatic epilepsy) differences appear to exist where the various diagnostic groups are concerned. Seizures are observed most frequently among the groups of hemiplegia and tetraplegia; the incidence being 33 per cent and 22 per cent in the present material. As is apparent from Table 8, the unfavourable prognostic effect of

Table 8.
Relation between motor and intellectual progress, on one hand, and presence of epilepsy on the other hand in tetraplegia and hemiplegia.

	Tetraplegia		Hemiplegia	
	Satisfactory motor progress per cent	Satisfactory intellectual progress per cent	Satisfactory motor progress per cent	Satisfactory intellectual progress per cent
Seizures occur.	6	0	50	56
No seizures ..	30	43	53	84

symptomatic epilepsy is much greater in tetraplegia than in hemiplegia, in respect of both motor and intellectual development.

The prognosis as regards survival is good after the fourth year of life as the majority of deaths occur before this age, see Figure 8.

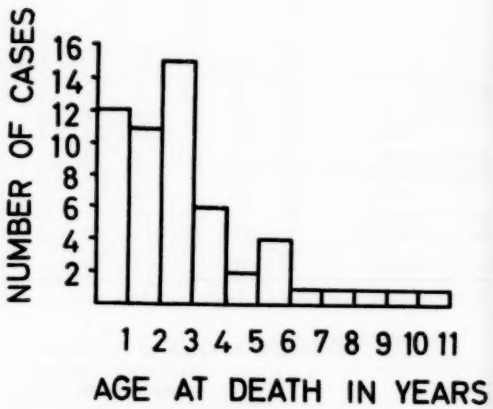

Fig. 8.
Age at death in years. Total of 55 deaths among 590 patients with cerebral palsy, comprising: 43 tetraplegia, 8 athetosis, 2 ataxia, 1 hemiplegia, 1 paraplegia.

In this material, no definite relation between the presumed etiology and the course of the disease could be demonstrated, perhaps because the individual groups are too small. Where the patients with athetosis are concerned, however, the cases which develop following severe neonatal asphyxia appear to have a poorer prognosis as regards motor progress than the cases which develop following severe icterus neonatorum; 2 out of 11 in the former group and 10 out of 15 in the latter group showed satisfactory motor progress.

INFLUENCE OF TREATMENT ON COURSE OF DISEASE

It would obviously be desirable to have a non-treated control group of exactly corresponding patients with the same degree of handicap, complications etc. In the present material, all the patients were treated, but as the treatment was carried out by the parents in their own homes, the treatment was of varying intensity and quality. On the basis of the intimate knowledge obtained concerning the parents from numerous conversations (see above) it was considered possible to subdivide the treatment into two large groups, satisfactory and unsatisfactory. It will be seen from Table 9 that satisfactory treatment of moderately severe cases is more frequently associated with satisfactory motor progress than is unsatisfactory treatment. Where slightly and severely handicapped cases are concerned, the difference, on the other hand, appears to be slight.

Table 9.
Connection between quality of treatment and result as regards motor progress.

Motor handicap	Satisfactory treatment			Unsatisfactory treatment		
	Progress			Progress		
	Good	Some	None	Good	Some	None
Slight	96	4	0	78	22	0
Marked	64	34	2	14	73	14
Severe	13	54	33	4	48	48

Percentage

The term treatment covers, as mentioned above, exercises and treatment with apparatuses in the home. Operative treatment has not influenced the result as the post-operative course is not included in the account. Medical treatment was only employed for a fraction of the period of observation and for a limited number of patients.

The extent to which the results are better when treatment is commenced early is not apparent in the present material, see Figure 1. The favourable effect of early treatment is probably obscured by the fact that the worst patients are first to be recognized and to have treatment instituted.

SUMMARY

1. In a material comprizing 203 cases of cerebral palsy, followed-up for more than three years, the possibility of estimating the prognosis from the etiology, symptoms and treatment was investigated.

2. The criteria used for diagnostic subdivisions, for the degrees of the various handicaps and for the quality of treatment are defined.

3. The motor handicap was marked or severe in 82 per cent of the cases; the intelligence was moderately or greatly retarded in 37 per cent and speech was affected in 64 per cent of the cases.

The relation between diagnosis and degree of motor, intellectual and speech handicap is represented graphically in Figure 2.

4. Seventy per cent of the children with normal intelligence attended normal schools. Speech therapy was considered necessary in 62 out of 203 children (31 per cent).

Twelve per cent of the cases were under the care of The Mental Deficiency Act.

5. Satisfactory motor progress was nearly always seen in cases with slight motor handicap. In cases with marked motor handicap the motor progress was clearly related to the degree of intellectual handicap. In cases with severe motor handicap satisfactory motor progress was rarely seen and only in cases with normal intelligence.

6. Certain symptoms and signs seem to be of prognostic value, *e. g.*, seizures and subnormal head circumference, especially in cases of tetraplegia, are associated with a poor progress.

7. The prognosis as regards survival is good after the fourth year (Figure 8).

8. Satisfactory treatment of moderately severe cases is more frequently associated with satisfactory motor progress than is unsatisfactory treatment. Where slightly and severely handicapped cases are concerned, the difference appears to be less, but not without importance.

INCOMPETENT COMMUNICATING VEINS OF THE LOWER LEG

PROBLEMS OF DIAGNOSIS

By CARL C. ARNOLDI

In the treatment of chronic venous insufficiency, the pathology of the communicating veins of the leg has been given an ever increasing importance.

As the late results of the various forms of surgical treatment are appearing, presence of insufficient communicating veins is being realised as a common cause of recurrence (3, 7, 8, 9, 10, 11, 16, 17, 20).

A considerable amount of work has been done to find a reliable method for diagnosing the state of the communicators prior to operation; the methods in use being phlebography in various forms, venous pressure measurements, and the clinical tests, among these, the "segmental" Trendelenburg test and Perthes' test.

A great step forward in the evaluation of the importance of the communicating veins of the lower leg, is Cockett's demonstration of the "ankle blow-out syndrome"; a state of insufficiency of the ankle perforators which are constantly found on the medial side of the lower half of the crus, draining the ulcer region here. A standard operation for varicose ulcers of this region has been developed and its usefulness has been confirmed by others (7, 8, 3).

Højensgård and Stürup (13, 14) emphasise the importance of the femoral communicators, especially the group joining the femoral

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Head: *H. Starklint.*

vein in Hunter's canal (henceforth called "Hunter communicators"). These authors regard the communicators on the lower leg as less important.

While varicosities of the internal and external saphenous veins are easily diagnosed clinically, insufficiency of the communicating veins gives but few clinical signs. In some cases a "blow-out" is found where a communicator pours out blood under a relatively high pressure into the subcutaneous vein. In my experience these globular blow-outs are most often found in the thigh (Hunter communicators) while they are more difficult to demonstrate on the lower leg.

Insufficiency of the ankle perforators may be diagnosed clinically by the presence of a "venous flare" a collection of tiny veins situated on the inner side of the foot and ankle, generally in the form of a half circle (see Figs. 1—2). According to Cockett & Jones (7) this is an important warning of a preulcerous state.

Cockett & Jones (7) are of the opinion that an insufficiency of the communicating veins of the lower leg, including the ankle perforators, is secondary to a thrombosis of the neighbouring deep veins. In a not unimportant number of cases this thrombosis has not given clinical signs and symptoms, and even a very throrough past-history fails to bring it to the memory of the patient. So a subclinical state of deep thrombosis is assumed to have taken place.

Recent investigations (4, 12, 15, 19) have, however, thrown some light on the etiology of the "state of varicosis" as such. In a previous paper (4) the author has shown a very characteristic relation between the age of menarche and the occurrence of varicosis, the later age-groups having a very high percentage of primary varicose veins, the very early age groups having a very low incidence of varicosities. This and other factors seem to point to a hormonal primary factor in the etiology causing at some time a venous dilation. When this is established the secondary hydrostatic factors come into play and produce the well known late state of varicosis.

In a previous paper (3) the author has given some preliminary results from a study now in progress concerning the heredity of varicosis.

The material then collected comprised 56 cases of ulcus cruris, men as well as women. All ulcers appeared in persons with a strong family history of varicosis and none were found in families without varicosities. The average menarche age of the families with ulcers was considerably higher than the average menarche age of the families with varicose veins but no ulcers. Finally the group without varicosities had a very low menarche age (Table 1).

Primary varicose veins were found to be far more frequent among women with a late menarche, and from the figures in Table I it seems as if the families with a tendency to late menarche, also have a more pronounced tendency to chronic venous insufficiency (ulcus cruris) among men as well as women.

Table 1.
Relation between familial menarche age and the degree of venous insufficiency.

Families	Number of families	Number of women	Average menarche age
— varicosities	22	113	13.2
— ulcers			
+ varicosities	37	199	14.5
— ulcers			
+ varicosities	17	89	15.0
+ ulcers			

In the available literature nothing has been published concerning any tendency to thromboembolic disease in any special groups of patients.

According to most modern authors a large percentage of leg ulcers are due to an earlier thrombosis of the deep veins of the leg. The percentage of ulcus cruris post-thromboticum varies with the different authors. Some figures from various authors are shown in Table 2.

Table 2.

Author	Number of ulcers	Percentage of cases with previous thrombosis
Bauer, 1952 (5)	38	87 per cent
Birger, 1947 (6)	432	40 per cent
Anning, 1952 (2)	715	80 per cent

In function and structure there is no essential difference between the proximal ends of the internal and external saphenous veins, and the entrance of the communicating veins and the ankle perforators into the deep veins of the leg. In all cases valves are preventing a back flow into the subcutaneous part of the venous system.

The ankle perforators, which in quite a number of cases have no anastomosis to the internal saphenous vein, can in fact, without any mental effort be regarded as a separate "third" saphenous system.

It is an established fact that a certain number of leg ulcers are due to the sequelae of deep thrombosis, and it is quite possible that these patients all have insufficient communicating veins and ankle perforators, due to local thrombotic destruction of the valves at the entrance to the deep veins (Fig. 1).

It is, however, equally possible that an insufficiency of these valves may be due to the same factors which are responsible for the primary varicosis of the saphenous veins (*vide supra*), especially where no past history of deep thrombosis can be coaxed from the patient. One of these factors may be the above mentioned hormonally conditioned primary venous dilatation supposed by King and supported by the author (15, 4).

From the figures shown in Table I where the relation between the degree of venous incompetence and the age of the menarche seems to be very striking, a further theoretical step might be taken: taking the indications of the figures at full value, it may seem as if a common factor of hormonal origin might be responsible for primary varicosis as well as for the tendency to thrombo-embolic disease.

The author is aware that this theory is far from proven, but it seems as if the problems involved are well worth investigation.

PERTHES' TEST

The new knowledge of the communicating veins of the lower leg and especially the ankle perforators, throw some doubt on the clinical usefulness of Perthes' test when it comes to the differentation of a state of previous deep thrombosis from "primary" varicosis of the communicators.

The historical interpretation of Perthes' test was: a positive test means patent deep veins, while a negative test indicates a block of the deep veins. Consequently the subcutaneous veins were regarded as necessary collaterals.

Højensgård (13) has most clearly shown that in the great majority of cases, failure of the veins to empty their blood into the deep veins means patent veins with valvular insufficiency due to recanalisation after deep thrombosis. According to this view, a negative Perthes' test is equivalent to past or present thrombosis of the deep veins of the leg.

Now it is quite clear that in a state of insufficiency of some communicating vein, distal to the compression used in Perthes' test, a failure of the veins to empty may be due to a back-flow through such an incompetent communicator. This is easily understood when we regard the case of post-thrombotic valveless deep veins with a high venous pressure, during rest as well as during muscular activity (14, 18). (See Fig. 1).

As long as the blood is flowing through the deep veins all valves must — of necessity — be open and the hydrostatic pressure at any given point must be equal to the difference in level between this point and the right auricle of the heart.

In the case where the deep veins are normal, but the valves of the communicating veins incompetent (see Case No. 1) the negative Perthes' test can easily be explained as caused by a back-flow of blood from the deep veins through the incompetent communicator into the subcutaneous veins, the blood being "blown" out by the higher hydrostatic pressure in the deep veins (see Fig. 2).

When an incompetent ankle perforator is cut during operation with the patient in the Trendelenburg position, the vein will bleed (back-flow). The subcutaneous saphenous veins will be collapsed in this position. When the patient is asked to contract his soleus muscle, small spurts of blood will be seen, as the contractions of the ensheathing muscle force the blood towards the point of least resistance. Consequently insufficiency of the ankle perforators must have a greater effect on the capillary pressure in the ulcer region than a saphenous incompetence.

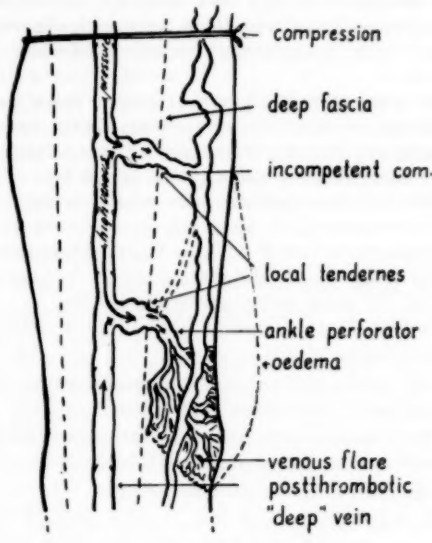

Fig. 1.
"Secondary varicosis" with incompetent communicating veins and ankle perforators as a late result of deep thrombosis. Perthes' test negative.

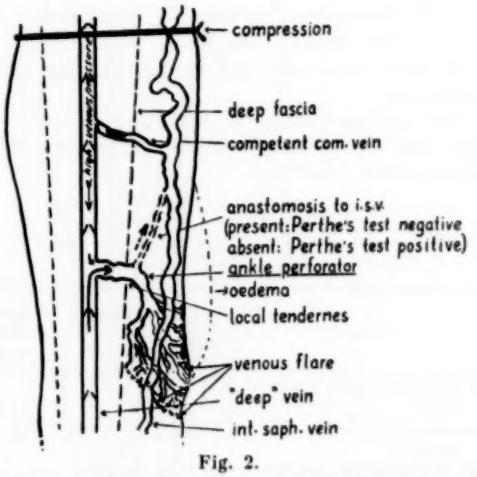

Fig. 2.
"Primary varicosis" of internal saphenous vein and ankle perforators. Normal deep veins. Perthes' test negative or positive according to the presence or absence of anastomoses between the incompetent ankle perforators and the saphenous system. In a case of this type the venous pressure will not show a definite fall to post-capillary levels until V a (cf. Fig. 3 and Case no. 1).

This corresponds very well with the fact that in our series a venous flare was only found together with incompetent ankle perforators. (Table 4).

Thus a negative Perthes' test might mean — theoretically at least — not a post-thombotic state, but a state of "primary varicosis" of one or more of the communicating veins of the lower leg.

In the not unexeptional case where a set of ankle perforators have no anastomoses to the internal saphenous vein a positive Perthes' test may be found with exactly the same state of "primary varicosis" of these ankle perforators. (Fig. 2).

According to this theory a positive Perthes' test may mean:

1) Normal deep veins and no insufficiency of communicators and ankle perforators.

2) Normal deep veins but insufficiency of a non-anastomosing set of ankle perforators.

A negative Perthes' test may mean:

1) Thrombosis of the deep veins present — deep veins blocked.

2) Post-thrombotic patent deep veins with no valvular function.

3) Insufficiency of communicating veins:

a) secondary to deep thrombosis (Fig. 1).
b) idiopathic ("primary") insufficiency of the valves. (Fig. 2).

4) Rigid vein walls preventing the veins from collapsing.

The outcome of this is, that the value of Perthes' test is doubtful, especially in patients with ulcus cruris. (Table 3).

Table 3.
The results of Perthes' test in various types of venous insufficiency.

Group	Ulcer patients	Positive Perthes' test	Negative Perthes' test
I. Previous deep thrombosis. Incompetent ankle perforators.	3	0	3
II. Incompetent saphenous veins. — deep thromb. — incomp. ankle perforators.	4	4	0
III. Incompetent ankle perforators. — deep thrombosis.	10	3	7
IV. Incompetent com. veins elsewhere in the crus. — deep thrombosis	2	1	1
Total	19	8	11

TRENDELENBURG's TEST

The "segmental" Trendelenburg test is the best means for a clinical evaluation of the presence of communicating veins of the upper leg, but according to the authors experience, of little use when it comes to the communicating veins of the lower leg, and quite useless where the ankle perforators are concerned.

This view is supported by Massell & Ettinger (17). In their series only 16 per cent of the existing incompetent communicators in the lower leg were found by the segmental Trendelenburg's test.

PHLEBOGRAPHY

A number of papers on the use of phlebography in the diagnosis of insufficient communicating veins have been published (8, 17, 18, 20). It is not at all difficult to obtain very good pictures of the veins of the lower leg, including the communicating veins, but the difficulty lies in determining whether such a vein is competent or not, that is, the direction of the blood-flow. Various methods have been developed but none of them quite satisfactory in this respect.

VENOUS PRESSURE

Investigations into the venous pressure in the deep and subcutaneous veins during rest and muscular activity have been a very valuable help in the research on venous pathology (14, 18). The technique, however, has in most cases prohibited the clinical use of this method. It must therefore be regarded as a very welcome help in the daily practise, that Dohn (9) has developed a simple method, using for a manometer the Scandinavian Standard Infusion set. The technique is very simple and sufficiently accurate for a routine clinical use. The reader is referred to Dohn's articles for details.

OWN INVESTIGATIONS

During the last ten months a method of diagnosing the incompetent ankle perforators and communicators of the lower leg has been in use here. The method consists of a clinical evaluation combined with phlebography and venous pressure measurements with a modified Dohn technique. Our findings have been controlled by operation. The results are shown in Table 4.

A thorough past history including inheritance of varicose veins and leg ulcers, age of menarche and signs and symptoms of previous deep thrombosis, has been compiled in each case. The Trendelenburg and Perthes' tests were all evaluated by the author personally.

Special notice was taken of any "blow-outs" and of the presence or non-presence of any venous flare. (When this is noticed on the inner side of the foot, Cockett's operation for incompetent ankle perforators is undertaken in connection with stripping of the varicose saphenous veins, even when there is no sign or history of leg ulcer, and also in cases where phlebography and venous pressure measuring cannot be performed for one reason or the other.).

Table 4.

27 cases of ulcus cruris and pre-ulcerous venous insufficiency grouped according to the clinical pictures, the results of phlebography, venous pressure measurements and the findings during operation.

Group	Ulcers	Venous flare no ulcer	Verified by phlebography	Verified by venous press.	Verified by operation
I. Previous deep thrombosis. Incompetent ankle perforators.	3	2	4	5	5
II. Incompetent saphenous veins. — deep thromb. — incomp. ankle perforators.	4	0	2*)	4	4
III. Incompetent ankle perforators. — deep thrombosis.	10	5	13	14	15
IV. Incompetent com. veins elsewhere in the crus. — deep thromb.	2	1	2	3	3
Total	19	8	21	26	27

*) Two cases in this group had phlebograms suggestive of incompetent ankle perforators. At operation these were found to be competent (small size — no retrograde bleeding).

A further diagnostic aid in the clinical diagnosis of incompetent ankle perforators is the circumscribed tenderness which very often is found, where the perforator emerges through the deep fascia. We do not know the reason for this tenderness but in our experience it is never found in this region unless the perforator is incompetent.

Phlebography.

After experimenting with various techniques in phlebography we have found the method advocated by Cockett & Dodd (8) most useful for demonstrating the ankle perforators and the communicating veins of the lower leg. For the visualisation of the deep veins of the leg, Højensgårds method (13) was found to give the best results. We have added the Valsalva manoeuvre.

For showing the ankle perforators, a piece of rubber tubing is placed slightly proximal to the middle of the lower leg. The patient is in the erect position. Twenty ml of Diodone 35 per cent is injected slowly over a period of 60 seconds into a vein on the medial side of the dorsum of the foot. Antero-posterior exposures are made half a minute after the start of the injection, and again at one minute, immediately after the injection is completed.

In the modified Højensgård technique an injection of 20—40 ml of Diodone 35 per cent is made as quickly as possible, with the patient in the erect position. Two pieces of rubber tubing are placed at the ankle and just below the knee. Antero-posterior and lateral exposures are taken at different levels.

During exposure, the patient is asked to blow out as hard as he can while pinching his nose and closing his lips firmly (Valsalva manoeuvre). We find the addition of this simple trick a definite improvement on the original technique.

Venous pressure.

For a description of the apparatus and the original technique, the reader is referred to Dohn's article (9).

For our use a routine method has been developed: during the measuring the patient is in the erect position. A wide calibered needle is introduced into a vein on the medial side of the foot. Sometimes this has been impossible and in these cases the needle has been placed in the internal saphenous vein at the level of the ankle. This has, however, been an exception.

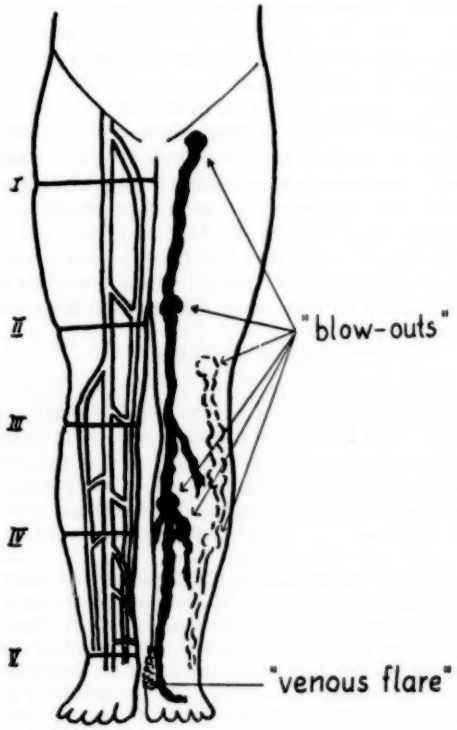

Fig. 3.

Compression levels during venous pressure measurements. Location of the most constant communicating veins and the ankle perforators.

The measurements of venous pressure are taken in the following order (compare Fig. 3): first the pressure is measured while the patient is standing at absolute ease, and then again after 40 seconds of "marking time" (rhythmic con-

traction of the soleus muscle). These first measurements are taken without compression of any kind. (O and Oa). A fall in venous pressure to the capillary level during "walking" would have indicated an absolutely sufficient deep and subcutaneous venous system. No such results were found, however, as no "normal" patients are included in this series.

Secondly a tourniquet is placed just distal to the fossa ovalis, and the same procedure is repeated (I and Ia). A fall in venous pressure, after muscular activity, to near the capillary level is assumed to mean an insufficient internal saphenous vein, the rest of the venous system being largely competent (cf. Case No. 2).

Further measurements are taken with the tourniquet placed just above the knee (II and IIa), excluding the "Hunter communicators"; immediately below the knee, excluding the external saphenous vein (III and IIIa). Next the tourniquet is placed slightly above the middle of the lower leg (IV and IVa) above the level of the ankle perforators and the most important lateral communicator. Finally measurements are taken with the tourniquet placed just above the ankle, below the level of the middle ankle perforator (V and Va).

For our use the exact values of pressure are inessential. A wide interval of pressure is allowed before a definite fall is assumed to have taken place (see Cases No.s 1 and 2). In experienced hands the measuring of venous pressure in the manner described can be done in 15 minutes.

In nearly every case the final venous pressure fell to about 35—40 cms of citrate, roughly corresponding to the expected post-capillary pressure.

CASE HISTORIES

Two very typical cases are shown below as representatives of two forms of "primary varicosis". The first in an example of insufficiency of both saphenous systems as well as the ankle perforators (Group III, Table 4). In Case 2 only the internal saphenous vein was incompetent (Group II, Table 4).

Case No. 1.: 58 years old male entered hospital for treatment of pronounced varicose veins. No past history of thrombosis or superficial phlebitis. Some 10 years ago injection treatment without effect. Never induration or ulcer. Complaining of heaviness, tiredness and nightly cramps. Left leg operated on 2 years previously a.m. Foote. No signs af varicosis present here.

Segmental Trendelenburg's test: no signs of communicating veins on the thigh. Perthes' test negative. Venous flare present on the medial side of the right foot. No induration or ulcer.

Phlebography: deep veins somewhat dilated but with abundance of apparently sufficient valves. Subcutaneous veins tortuous and dilated. Eight cms proximal to the medial malleolus a large communicating vein; 12 cms from the ankle another smaller communicating vein.

Venous pressure: O 136 cm, I 126 II 122 III 119
Oa 116 cm, Ia 116 IIa 120 IIIa 108
IV 135 V 87
IVa 118 Va32

Operation: the external and internal saphenous veins were exstirpated by stripping *a.m.* Foote and an incision *a.m.* Cockett was made behind the margo medialis tibiae. Three insufficient ankle perforators were found all with anastomosis to a branch of the internal saphenous vein. The upper and middle ankle perforator had a diameter of over one cm.

This is a very typical case of all-out insufficiency of both saphenous systems and ankle perforators, in this case anastomosis to the internal saphenous vein. Deep veins normal. Perthes' test negative (Fig. 2).

Case No. 2.: 41 years old postman entered hospital for treatment of varicose veins of the left leg. No history of thrombosis or phlebitis. No previous treatment. Complaining of heaviness, tiredness, cramps at night and evening oedema. No history of ulcer or induration.

Segmental Trendelenburg's test: no signs of incompetent communicating veins on the thigh. Perthes' test moderately positive. No venous flare. No indurations or leg ulcer.

Phlebography: deep veins of the crus normal with abundance of valves. On the medial side of the leg tortuous dilated veins. No visible communicating veins.

Venous pressure: O 130 cm I 97 cm
Oa 126 cm Ia 38 cm
(no further measurements undertaken).

Operation: extirpation of internal saphenous vein a. m. Foote. Dissection of the varicose plexus below the knee showed no signs of communicating veins here.

This is a case of primary varicosis of the internal saphenous vein. Diagnosis confirmed by phlebography and the figures of venous pressure.

DISCUSSION

As will be seen from Table 4, the results gained from measuring the venous pressure in the way described above seems to be a little more accurate than those obtained from phlebography. A notable fall in pressure between the levels four and five has in all cases been proved by operation to be due to an insufficient communicating vein or ankle perforator on the lower leg.

What this method cannot show us is, however, exactly where the communicator at fault is situated. This is the domain of phlebography. While the ankle perforators are almost constantly found in front of the medial side of the soleus muscle behind the medial margin of the tibia, no such constancy is present where the lateral perforators and the rest of the communicating veins are concerned.

A venous flare has been present in all cases where incompetent ankle perforators have been diagnosed by phlebography, venous pressure measuring or through operation. As our experience has widened we have come to regard this symp-

tom as equivalent to the presence of a pressure leak somewhere on the lower half of the crus and an absolute indication for the use of the combined phlebography-venous pressure method.

In our view, a standard operation of the Cockett or Linton type in all cases of ulcers is not justified, for two reasons: First, a certain group of ulcers are definitely due to saphenous insufficiency alone (the simple "ulcus cruris varicosum"). Secondly, any incision in this ulcer bearing region, which in most cases is infested with oedema and induration, should be restricted to the utmost minimum. With an accurate preoperative diagnosis as to the location of the pressure leaks, surgical traumatisation is kept at a minimum.

As will seen from the figures in Table 3, Perthes' test is incapable of differentation between a state of post-thrombotic deep vein insufficiency and incompetent communicating veins of the lower leg. The majority of phlebograms showing incompetent communication veins and ankle perforators have had deep veins of the crus with no visible signs of earlier thrombosis.

The percentage of post-thrombotic ulcers is very low in this material (16 per cent). It is realised, however, that this does not give a true picture of the percentage of post-thrombotic ulcers seen here. Among the leg ulcers treated conservatively with pressure bandages, a larger number of post-thrombotic ulcers may be found; these patients have generally been poor operative risks, many of them bedridden for long periods. Quite a number of them have been subjected in vain to various forms of injections and conservative treatment with different ointments for several decades, and quite naturally they have lost all belief in medical help.

All these factors taken into consideration the fact remains, however, that our experience has told us that the true post-thrombotic ulcer is far less common than the figures given by some modern authors (Table 2).

This has a bearing on our therapeutic optimism, but whether the promises will be kept is a question, which only can be answered when follow-up studies over a number of years have been made.

The tendency — where phlebography and venous pressure measurements are concerned — has mostly been to refer these investigations to the experimental research laboratory, finding no clinical use for them except in very special cases (1).

The results of the various forms of surgical treatment of varicose veins and ulcus cruris have shown an ever increasing number of satisfactory results, but even so, recurrences do take place and unfortunately mostly in patients with leg ulcers.

In order to lessen the number of recurrences, no other way is open, but to make clinical use of the special knowledge collected in the laboratory of the researchworker, and the intention of this paper has been to show a clinically useful method which gives promise of a high degree of accuracy in diagnosing the all-important incompetent communicating veins of the lower leg, especially the ankle perforators.

SUMMARY

The value of the Perthes' test is investigated. The interpretation of a positive or negative result is evaluated. The possibility of a primary varicosis of the communicating veins is considered.

A method of diagnosing the incompetent communicating veins by a combination of phlebography and venous pressure measurements is described. The results have been controlled through operation. A very satisfying correlation was found.

According to these investigations the value of the Perthes' test is doubtful when it comes to diagnosing post-thrombotic venous insufficiency as no differentation is possible between this state and cases of "primary varicosis" of the communicating veins and ankle perforators of the lower leg.

It is the author's opinion that where there are signs of chronic venous insufficiency (oedema-ulcus cruris — venous flare) this combination of pressure measuring and phlebography should be performed, as only in this way does he see a means of reducing the number of recurrences after the various forms of surgical treatment.

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PHYSIOLOGICAL ACTIVITY CHANGES IN THE RETINAL GANGLION CELL

SUMMARY OF THESIS

By KNUD BECH

In recent years, a number of works have been published dealing with the metabolism of nucleic acid in the ganglion cells (Einarson, Einarson and Lorentzen, Einarson and Krogh, Hartelius, Hochberg) as well as in the secretory cells (Oram, Weber) when these are exposed to stress. All the works mentioned above are based upon investigations of cells stained with Einarson's gallocyanin-chromalum staining method. This method of staining is highly selective and progressive when determination of the content of nucleic acid in a cell is concerned.

The majority of these investigations were undertaken during a period in which apparatus sufficiently finely graduated to register the slight changes in the content of nucleic acid in the cells which might be anticipated to occur under physiological conditions was not available. As very finely graduated apparatus (Hansen and Einarson) for relative quantitative measurement of nucleic acid in the individual cells is now available, it was decided to investigate the metabolism of nucleic acid during physiological conditions.

The method of measurement consists of registering the quantity of light absorbed when light of a constant power is sent through cells stained with gallocyanin-chromalum.

Only one organ in the body, *viz.*, the eye, is suitable for investigations of this nature. By keeping the experimental animal in darkness, every adequate stimulus can be excluded from the eye and a condition of absolute rest of the ganglion cells of the eye thereby obtained. Subsequently, by exposing the animal to daylight for periods of varying length after 24 hours in darkness, changes in the content of nucleic acid such as occur during normal conditions of life may be produced.

Out of the many types of nerve cells in the eye, it was decided to employ the cells of the stratum ganglionare of the retina. In this layer, however, several different types of ganglion cells are present and as no previous typological classification of these cells particularly in respect of their appearance when stained according to Nissl's method was available, it was necessary first to undertake such a classification. The cells were classified into three types, partly in respect of size and more particularly according to their contents of basophilic substances. Out of these types, large cells very similar to ordinary large multipolar ganglion cells were chosen as the object of the experiment. These cells were then investigated after the experimental animal had been kept in darkness for varying periods and it was found that the cells attained their condition of absolute rest after a period of rest of 24 hours.

The same type of cell was then investigated after the animals had been exposed to physiological influence, *i. e.* daylight, for varying periods.

By the methods of measurement mentioned two significant observations were made. Firstly during physiological conditions the same metabolism of nucleic acid in the ganglion cells occurs as during stress but of a far lesser magnitude. Secondly, further evidence to support Einarson's theory of initial chromophilia was obtained. This theory states that immediately a cell is exposed to influence of one sort or another, excess production of nucleic acid occurs which exceeds the immediate requirements of the cell and thereafter the content of nucleic acid is adjusted to a somewhat lower level.

To obtain significant results with these investigations it is necessary to undertake measurements on a large number of cells as, under all circumstances, the nerve cells in any organ are in varying stages of chromophilia but with varying percentage distributions of these stages. In the experiments mentioned, measurements on 400—800 cells in each experimental series were undertaken.

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